

EXHIBIT A

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Fenlon

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(45) **Date of Patent:** **Mar. 13, 2012**

(54) **METERED-DOSE INHALER**

(58) **Field of Classification Search** 235/91;
128/200.23
See application file for complete search history.

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(*) Notice: Subject to any disclaimer, the term of this
patent is extended or adjusted under 35
U.S.C. 154(b) by 159 days.

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§ 371 (c)(1),
(2), (4) Date: **Sep. 23, 2009**

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(65) **Prior Publication Data**

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Related U.S. Application Data

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2, 2007.

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(30) **Foreign Application Priority Data**

Apr. 11, 2007 (GB) 076999.0

(57) **ABSTRACT**

A metered dose inhaler dose counter, the counter includes: an actuator; a rotary gear wheel having a plurality of ratchet teeth; a driver for driving the rotary gear in a step-wise fashion in response to displacement of the actuator; a pawl that prevents reverse rotation of the rotary gear; and a display coupled to the rotary gear.

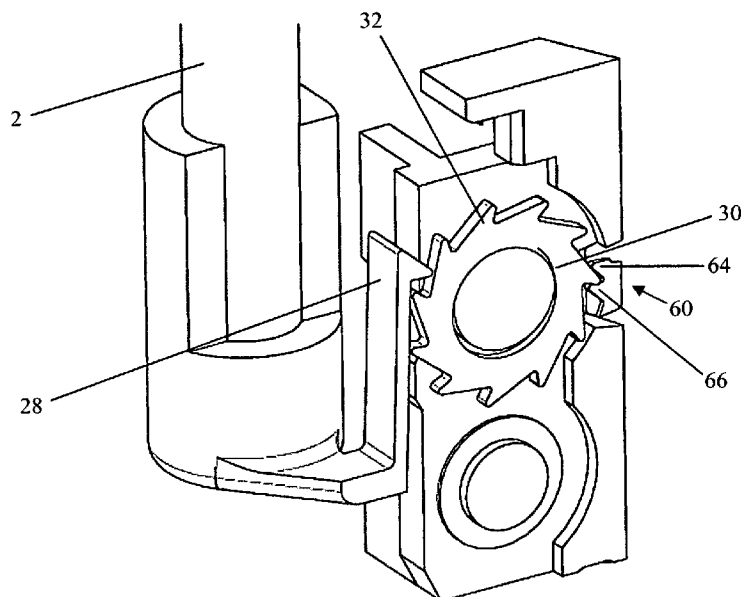
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A61M 11/00 (2006.01)

(52) **U.S. Cl.** **235/91 R; 128/200.23**

19 Claims, 8 Drawing Sheets

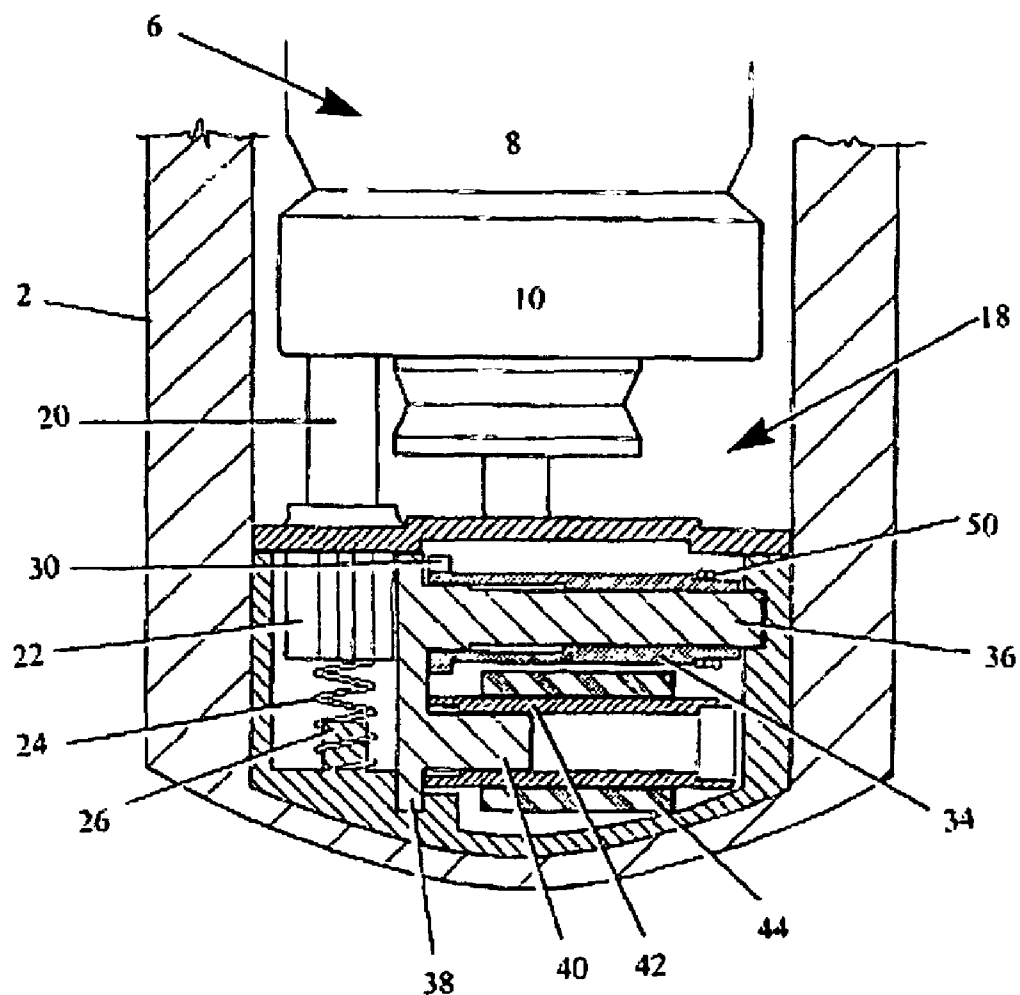


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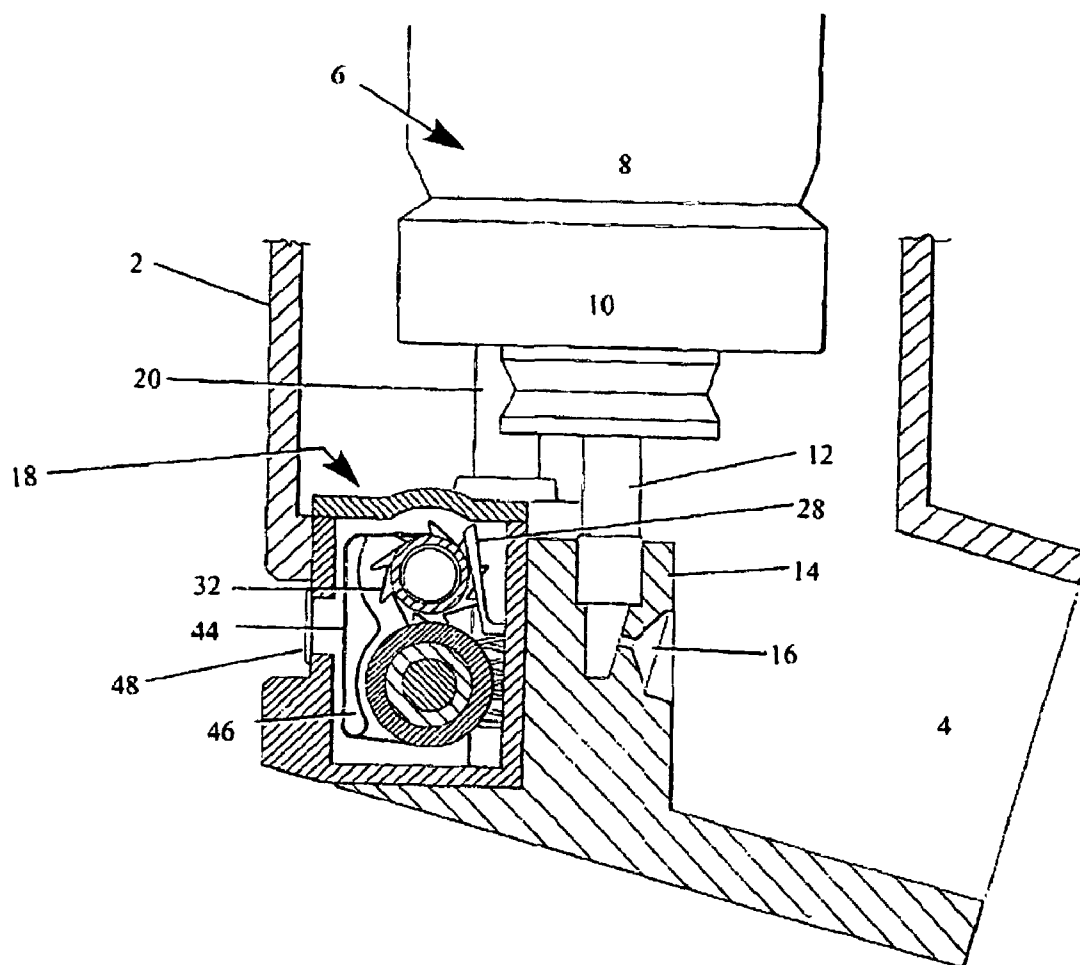
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(Prior art)

Fig. 1



(Prior art)

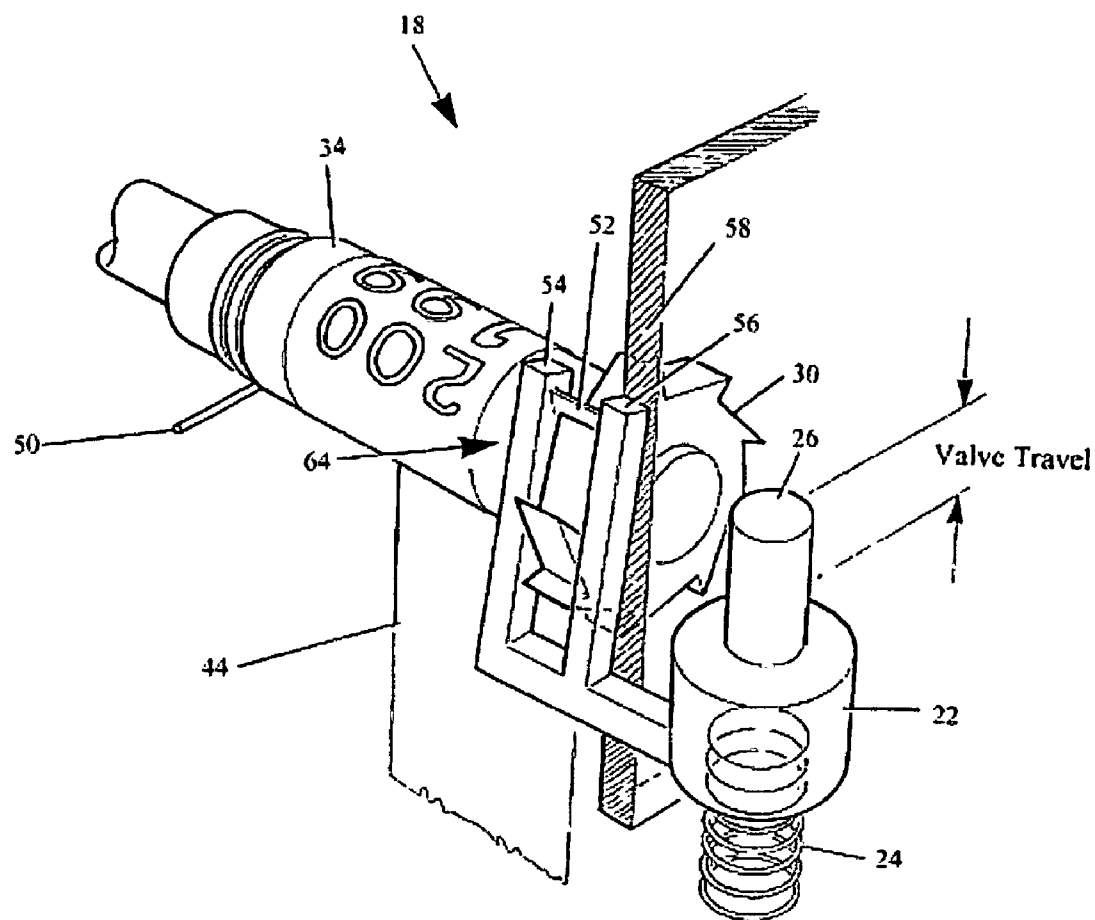
Fig. 2

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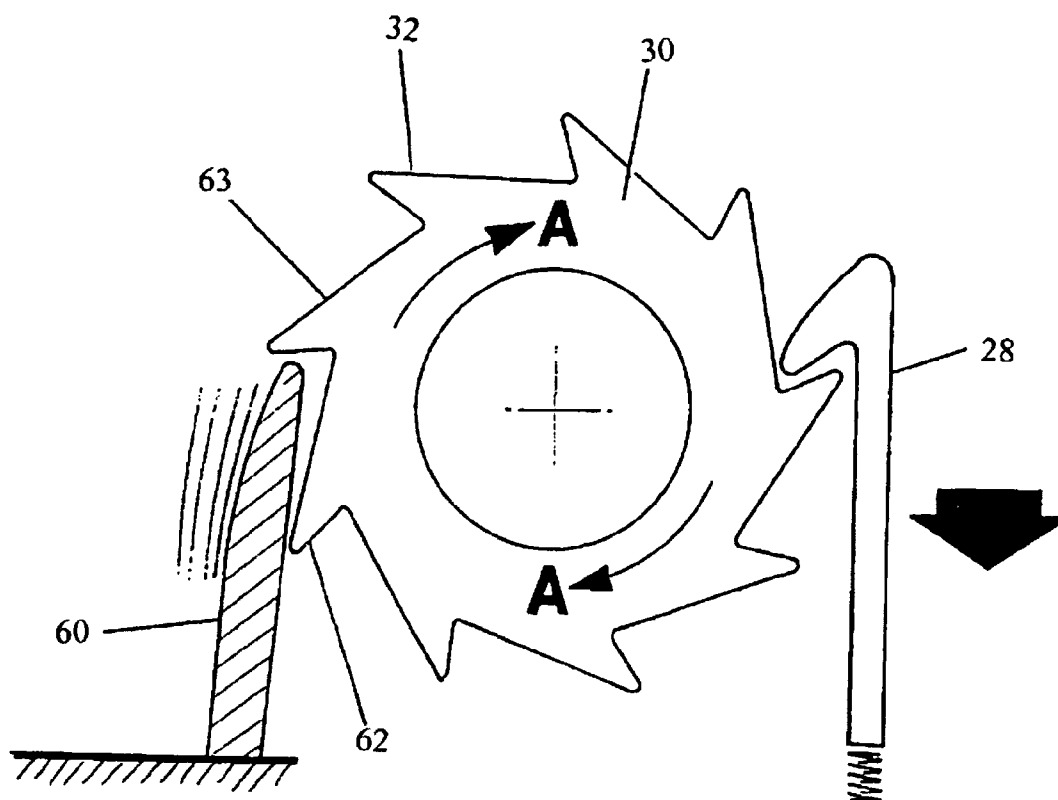
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(Prior art)

Fig. 3



(Prior art)

Fig. 4

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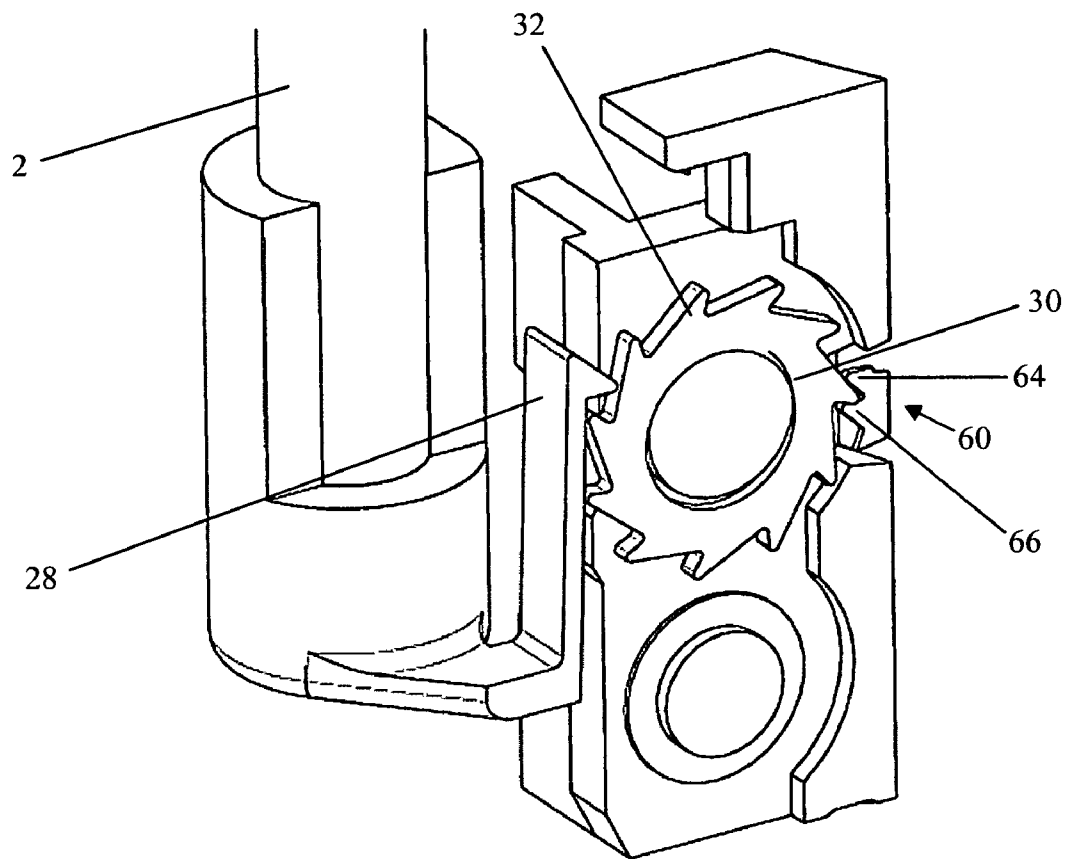


Fig. 5

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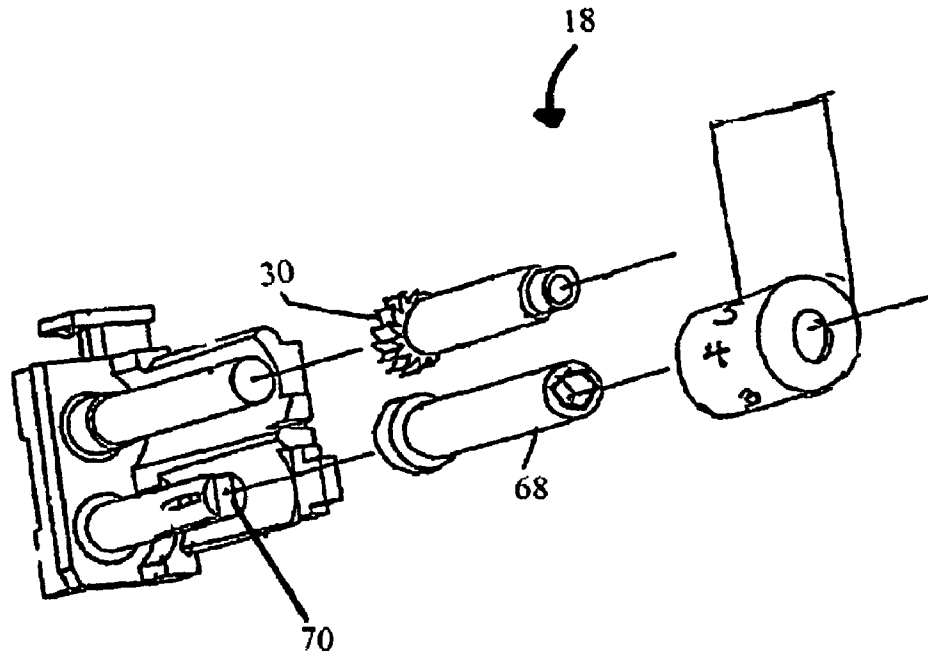


Fig. 6

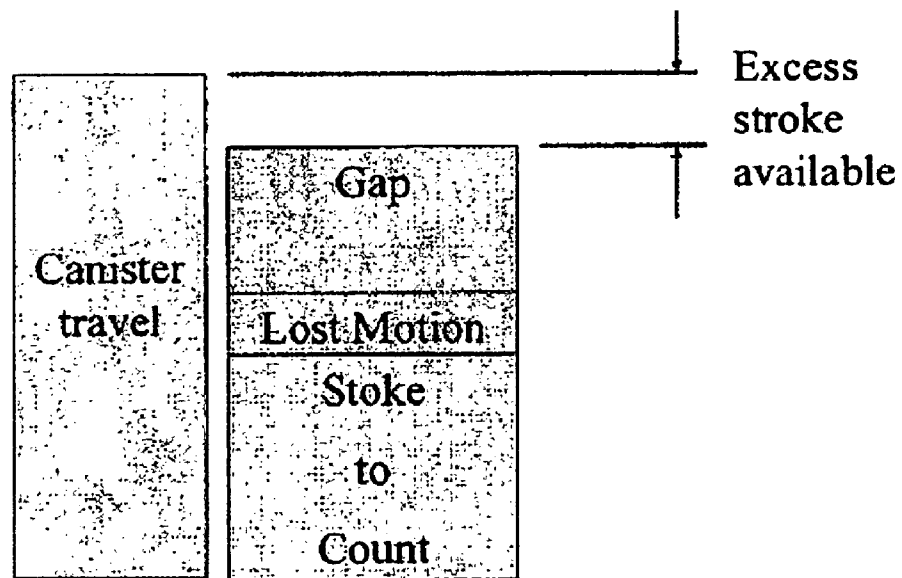


Fig. 7

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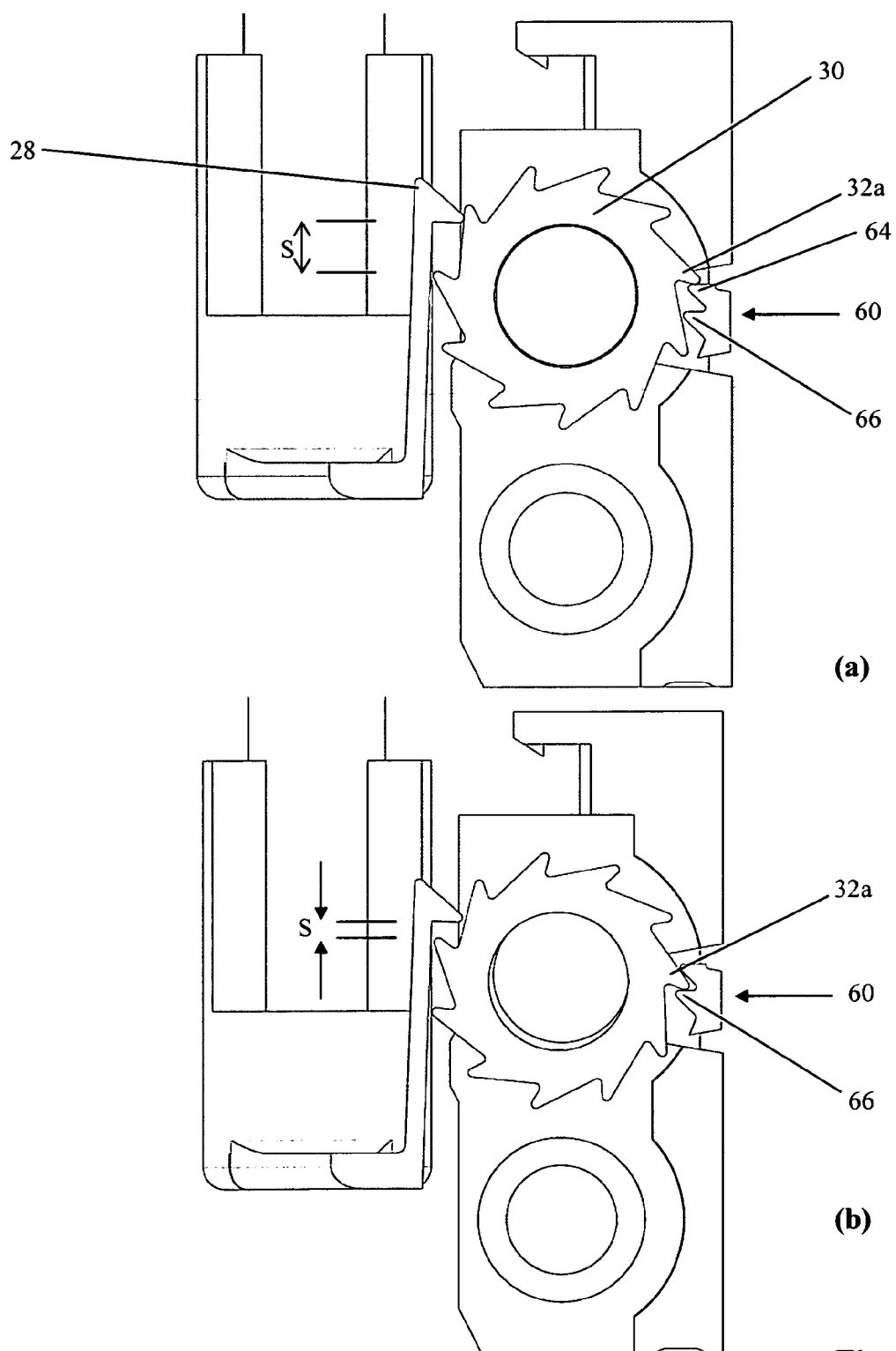


Fig. 8

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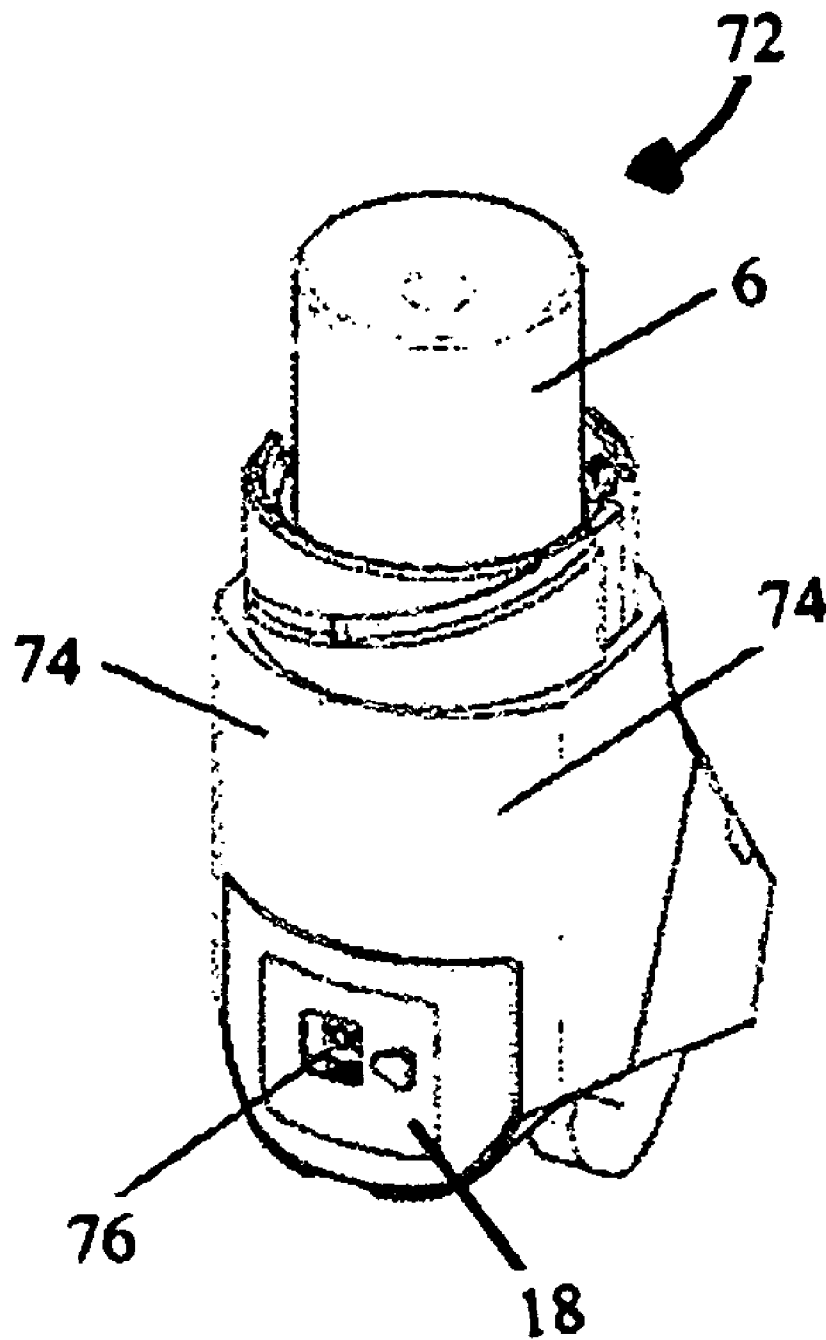


Fig. 9

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METERED-DOSE INHALER**CROSS-REFERENCE TO RELATED
APPLICATIONS**

This application is the U.S. national phase application of PCT International Application No. PCT/EP2008/002590, filed Apr. 1, 2008, which claims priority to U.S. Provisional Patent Application No. 60/921,320, filed Apr. 2, 2007, and GB Application No. 0706999.0, filed Apr. 11, 2007, the contents of such applications being incorporated by reference herein.

FIELD OF THE INVENTION

This invention relates to a metered-dose inhaler and in particular to a dose counter for a metered-dose inhaler, the counter comprising: an actuator; a rotary gear; a driver for driving the rotary gear in a step-wise fashion in response to displacement of the actuator, the rotary gear comprising a wheel mounted on a spindle which wheel having a plurality of ratchet teeth around its periphery; a pawl to prevent reverse rotation of the rotary gear; and a display coupled to the rotary gear, the display having a visible array of incrementing integers on a surface thereof indexable by a single integer in response to each step of the step-wise rotary motion of the rotary gear; wherein the pawl comprises at least two ratchet teeth which are radially spaced such that one of the teeth engages with the ratchet teeth of the wheel following each step of the step-wise rotary motion of the rotary gear.

BACKGROUND OF THE INVENTION

Metered-dose inhalers include pressurised metered-dose inhalers (of both manually operable and breath-actuated types) and dry-powder inhalers. Such metered-dose inhalers typically comprise a medicament-containing vessel and an actuator body having a drug delivery outlet.

The medicament-containing vessel may be a pressurised canister containing a mixture of active drug and propellant. Such canisters are usually formed from a deep-drawn aluminium cup having a crimped lid which carries a metering valve assembly. The metering valve assembly is provided with a protruding valve stem which, in use, is inserted as a tight push fit into a so-called "stem block" in the actuator body.

To actuate the conventional manually operable inhaler, the user applies a compressive force to the closed end of the canister. The internal components of the metering valve assembly are spring loaded so that a compressive force of about 15 to 30 N is required to activate the device.

In response to this compressive force, the canister moves axially with respect to the valve stem by an amount varying from about 2 to 4 mm. This degree of axial movement is sufficient to actuate the metering valve and cause a metered quantity of the drug and propellant to be expelled through the valve stem. This is then released into the mouthpiece via a nozzle in the stem block. A user inhaling through the drug delivery outlet of the device at this point will thus receive a dose of the drug.

Metered-dose inhalers as described above administer an accurate dose of medicament whenever required, which is particularly useful for users whose respiratory difficulties manifest themselves suddenly. Such has been the success of these devices that they are now used throughout the world.

A more recent development is the so-called "breath-operated actuator" which delivers a dose of drug through a mouth-

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piece in response to inhalation by the user. This type of arrangement is particularly convenient in circumstances where the co-ordination between user inhalation and manual depression of the aerosol canister is imperfect. For example, children sometimes lack the necessary co-ordination to achieve effective self-administration and, at times of respiratory distress, adult users may also experience poor co-ordination.

SUMMARY OF THE INVENTION

One of the drawbacks of self-administration from an inhaler is that users often experience difficulty in determining when the charge in the medicament-containing vessel has nearly run out since the contents of the medicament reservoir are typically invisible to the user. With aerosol canisters, part of the reason for this difficulty is that a surplus of propellant may remain in the canister even though the drug supply is nearly exhausted. Alternatively, the near-exhausted state may result in a surplus of drug in relation to propellant. Thus, the illusion is created that the inhaler is still capable of providing useful doses of medicament simply because the canister contains liquid. This is potentially hazardous for the user since dosing becomes unreliable and because few users routinely carry a back-up device.

Many users have several different inhalers for the treatment of a variety of conditions. Others keep inhalers at a number of different locations such as at school, home, work etc. In these circumstances it is particularly difficult for the user to keep track of the amount of usage extracted from each individual inhaler apparatus.

Clearly there is a need for a counter mechanism which enables users to assess how many doses remain in the obscured canister. Such a counter would ensure that users are warned when the inhaler nears exhaustion so that appropriate measures can be taken to avoid running out of medication. Moreover, if a dose counter can provide readability to a resolution of one dose, this can be used for compliance monitoring, either under hospital supervision or by parents and teachers assessing compliance by children in their care. In addition, there are regulatory requirements for metered-dose inhalers to have a dose counter in a number of countries.

WO 98/28033 discloses a dose counter suitable for use with the above-described metered-dose inhalers. FIGS. 1 and 2 reproduced herein from WO 98/28033 show the lower portion of a metered-dose inhaler. The inhaler comprises an actuator body 2 having a drug delivery outlet 4. An aerosol canister 6 extends into the lower portion of the actuator 2. The aerosol canister 6 is formed from a deep-drawn aluminium cup 8 to which a lid 10 is attached by crimping.

The lid 10 carries a metering-valve assembly having a protruding valve stem 12, the end of which is received as a tight push fit in a stem block 14 of the actuator body 2. Stem block 14 has a nozzle 16 communicating with the drug delivery outlet 4 so that, upon actuation of the metering-valve assembly, a charge of the drug is emitted through the nozzle 16 into the drug delivery outlet 4. Actuation of the metering-valve assembly is effected by causing downward movement of the aerosol canister 6 relative to the actuator body 2. This may be achieved through manual pressure exerted by the user against the upturned base (not shown) of the aerosol canister 6 or by automatic depression of the aerosol canister 6 in response to user inhalation in inhalers of the breath-actuated type. The mechanism of breath actuation does not form part of WO 98/28033 or the present invention and will not be described in further detail. A user inhaling through the drug

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delivery outlet **4** when the aerosol canister **6** is depressed will receive a metered dose of the drug.

A counter mechanism **18** includes an actuator **20** moulded from a plastics material, such as nylon, the actuator **20** having a boss **22** integrally formed at its base.

The underside of boss **22** is formed with a blind hole which receives a compression spring **24** mounted on an upstanding spigot **26** formed on a lower element of the counter chassis.

A driver **28** for driving a rotary gear in the form of a ratchet-toothed wheel **30** is integrally moulded with boss **22** of the actuator **20** and comprises a transverse hook element (not shown) mounted between two arms (only one visible in FIG. 2), the bases of which are conjoined to the boss **22**. The transverse hook is dimensioned and oriented to engage with ratchet teeth **32** formed around the periphery of the ratchet-toothed wheel **30** to rotate it in a forward direction.

The ratchet-toothed wheel **30** is integrally moulded with a first hollow axle **34** which is rotatably supported on a first spindle **36** that projects transversely from a chassis sub-element **38**. Chassis sub-element **38** also has a second spindle **40** projecting transversely therefrom on which a second hollow axle **42** is rotatably supported. A flexible tape **44** is wound around the second hollow axle **42** which serves as a supply spool and passes to the first hollow axle **34** which serves as a take-up spool (stock bobbin). A guide plate **46** forming part of the chassis sub-element **38** helps to guide the tape **44** in a smooth passage from the supply spool to the take-up spool. The surface of the tape **44** is marked with a progression of descending numbers which denote the number of doses remaining in the aerosol canister. Typically, the starting count is 200 and successive markings on the tape decrease by one. The spacing between successive markings is coincident with the indexing motion of the matching wheel **30** so that a new number appears in a window **48** provided in the inhaler housing **2** for each successive actuation.

The ratchet-toothed wheel **30** and integrally formed first hollow axle **34** are restrained from reverse rotation by a wrap-spring clutch **50** surrounding the hollow axle **34** at the end thereof remote from ratchet-toothed wheel **30**. One end (not shown) of the wrap-spring clutch **50** is braced against the counter chassis. The windings of the wrap-spring clutch **50** are oriented such that rotation of the first hollow axle **34** in a forward sense is not resisted by the spring coils. However, reverse rotation of the hollow axle **34** acts so as to tighten the spring coils around it, thereby causing the first hollow axle **34** to be gripped by the internal surface of the wrap-spring clutch **50** and hence restraint from reverse rotation.

FIG. 3 shows a preferred embodiment of the invention set out in WO 98/28033. The dose counter **18** comprises an actuator **20** having a boss **22** integrally formed therewith and driver **28** joined to the boss **22**. The underside of boss **22** is provided with a blind hole which receives a compression spring **24** that serves to return the actuator **20** to its rest position after depression thereof during actuation of the inhaler apparatus (not shown).

The driver **28** comprises a transverse hook **52** mounted between a pair of arms **54,56** which are joined at their bases by a web (not shown). The web is connected to the boss **22** of the actuator **20**. A combined actuator and driver assembly may be integrally formed, such as from a plastics material, e.g. as nylon.

In use, the transverse hook **52** engages with ratchet teeth **32** of a ratchet-toothed wheel **30** which is mounted on a hollow axle **34** serving as a take-up spool for a flexible tape display **44**. At the end of the hollow axle **34** remote from the ratchet-toothed wheel **30** is a friction clutch **50** which serves to

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restrain the axle **34** against reverse rotation and hence prevents reverse travel of the counter tape **44**.

A control surface **58** is depicted here as a see-through element so that the workings of the dose counter may be more clearly seen. The control surface **58** extends parallel to the direction of travel of the actuator **20** and is located adjacent the ratchet-toothed wheel **30** at a position which marks a chordal projection across one of the wheel faces. One of the support arms **56** of the driver **28** is in sliding contact with control surface **58**. This sliding contact serves to inhibit the natural tendency of the driver **28** to flex radially inwardly towards the axis of rotation of the ratchet-toothed wheel **30**. By preventing such radially inward flexure, the control surface **58** restricts the engagement and disengagement of the drive **28** with the ratchet-toothed wheel **30** so that the distance by which the ratchet-toothed wheel **30** rotates is limited to one tooth pitch. This condition is observed regardless of the extent of linear travel, or stroke, of the actuator **20**.

FIG. 4 shows a schematic view of a conventional ratchet gear and drive pawl arrangement which is used in the dose counter described in WO 98/28033. The arrangement uses a reciprocating driver **28** acting in a pushing sense to rotate a ratchet-toothed wheel **30** in the direction shown by the arrows A. A fixed pawl **60** acts to prevent reverse rotation of the ratchet-toothed wheel **30** by engagement against the trailing edge **62** of a ratchet tooth **32**. However, on forward rotation of the ratchet-toothed wheel **30** in the sense of arrows A, the fixed pawl **60** is capable of radially outward deformation, urged by the leading edge **63** of a ratchet-tooth **32**.

In this arrangement, if the ratchet-toothed wheel **30** is rotated by more than a single tooth pitch but by less than two tooth pitches for each reciprocating movement of the driver **28**, there is a degree of reverse rotation until the pawl **60** becomes engaged by the trailing edge **62** (as opposed to the leading edge **63**) of a ratchet tooth **32**. Thus, the rotation of the ratchet-toothed wheel **30** may be said to be "stepped".

The components of metered-dose inhalers are manufactured to a high technical specification. However, inevitable variations in the tolerances of the components can, in some circumstances, lead to failure of the dose counter of the type disclosed in WO 98/28033. The failure of the dose counter, although not common, makes the dose counter of the type disclosed in WO 98/28033 unsuitable for some applications. There is a requirement in the art, therefore, for a dose counter with a reduced failure rate.

Accordingly, a first aspect of the present invention provides a dose counter for a metered-dose inhaler, the counter comprising:

- an actuator;
- a rotary gear;
- a driver for driving the rotary gear in a step-wise fashion in response to displacement of the actuator, the rotary gear comprising a wheel mounted on a spindle which wheel having a plurality of ratchet teeth around its periphery;
- a pawl to prevent reverse rotation of the rotary gear; and
- a display coupled to the rotary gear, the display having a visible array of incrementing integers on a surface thereof indexable by a single integer in response to each step of the step-wise rotary motion of the rotary gear;
- wherein the pawl comprises at least two ratchet teeth which are radially spaced such that one of the teeth engages with the ratchet teeth of the wheel following each step of the step-wise rotary motion of the rotary gear.

The counter of the present invention thus provides a pawl having at least two teeth in which one and the same tooth engages with successive ratchet teeth of the wheel during the step-wise rotary motion of the wheel to prevent reverse rota-

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tion of the wheel (and hence the rotary gear). By providing alternative positions for engaging the ratchet teeth of the wheel, the pawl increases the range of tolerances in the manufacture of the various components of the inhaler which can be accommodated. This in turn significantly reduces the failure rate of the dose counter and, in particular, the likelihood of undercounting. Clearly, undercounting is particularly undesirable as it can lead to a patient believing that there are more doses left within the inhaler than there actually are.

BRIEF DESCRIPTION OF THE DRAWINGS

The present invention will now be described with reference to the accompanying drawings, in which:

FIGS. 1 to 4 show a dose counter for a metered-dose inhaler according to the prior art document WO 98/28033;

FIG. 5 shows elements of a dose counter according to the present invention;

FIG. 6 shows further detail of the dose counter according to the present invention;

FIG. 7 shows a schematic representation of journeys undertaken for indexing of the dose counter to occur;

FIG. 8 shows the wheel and pawl of the dose counter of the present invention in which the pawl is (a) operating from the first tooth and (b) operating from the second tooth; and

FIG. 9 shows a metered-dose inhaler containing the dose counter of the present invention.

DETAILED DESCRIPTION OF THE INVENTION

The dose counter of the present invention is based on that set out in FIGS. 3 and 4 described hereinabove except that the pawl 60 has been modified. Modification of the pawl followed an in-depth study of all of the components of the inhaler. Thus, as shown in FIG. 5, the dose counter 18 of the present invention comprises an actuator 20; a rotary gear (not shown in full in FIG. 5); a driver 28 for driving the rotary gear in a step-wise fashion in response to displacement of the actuator 20, the rotary gear comprising a wheel 30 mounted on a spindle (not shown), the wheel 30 having a plurality of ratchet teeth 32 around its periphery; a pawl 60 to prevent reverse rotation of the rotary gear; and a display (not shown) coupled to the rotary gear, the display having a visible array of incrementing integers on a surface thereof indexable by a single integer in response to each step of the step-wise rotary motion of the rotary gear.

The wheel 30 has a plurality of ratchet teeth 32 and preferably has 8-14 teeth (i.e. 8, 9, 10, 11, 12, 13 or 14), more preferably 9, 10, 11 or 12 teeth, and most preferably 11 teeth.

The radius of the wheel 30 measured from the centre of the wheel 30 to the tip of the teeth 32 will depend on the size of the components of the inhaler. Preferably the radius is from 1.5 to 3.5 mm, more preferably from 2.0 to 3.0 mm and most preferably 2.80 ± 0.05 mm.

As in the dose counter 18 of WO 98/28033, the dose counter 18 of the present invention preferably further comprises a control surface to regulate the position of engagement and disengagement between the driver 28 and the wheel 30. In addition, the driver 28 comprises a ratchet drive pawl and preferably the ratchet drive pawl is in the form of a straddle drive in which the element that engages the ratchet teeth of the wheel is supported between a pair of spaced apart support arms.

The pawl 60 comprises at least two ratchet teeth 64,66. Preferably, as shown in FIG. 5, the pawl 60 comprises two ratchet teeth 64,66 and no more. The at least two ratchet teeth 64,66 are radially spaced with respect to the ratchet-toothed

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wheel 30 such that one and the same tooth engages with the ratchet teeth 32 of the wheel following each step of the step-wise rotary motion of the rotary gear. Typically, one, and only one, of the ratchet teeth 64,66 on pawl 60 ever engages with the ratchet wheel.

FIG. 6 shows an exploded view of the dose counter 18 showing in addition to the previously described components, the stock bobbin 68 which is held taut by the action of the split hub 70. The split hub 70 avoids the need for a clutch spring as set out in WO 98/28033. Although the clutch spring could be used as an alternative or in addition to the split hub 70, in a preferred embodiment, the dose counter of the present invention does not include a clutch spring. The display is preferably an elongate counter tape 44 on which the dose count is printed or written, and more preferably the counter tape 44 is located on an indexing spool and the dose counter further comprises a stock bobbin to receive the counter tape as the indexing spool is advanced in a step-wise fashion.

In use, the operation of the dose counter 18 is as follows.

The user depresses the aerosol canister 6 which causes displacement of the actuator 20. In this embodiment, the actuator 20 is adapted to engage with the rim of the medication canister 6. The actuator 20 is operable by linear displacement from a first position to a second position and back to the first position and movement of the rotary gear occurs either during the displacement of the actuator from the first position to the second position or during the displacement of the actuator from the second position to the first position. In the embodiment shown in FIG. 5, the movement of the rotary gear occurs during the displacement of the actuator from the first position to the second position. In the embodiment shown, the actuator 20 comprises a spring-loaded plunger 22,24, the plunger being depressible against the return force of the spring loading when the actuator is caused to deliver a dose of medicament.

During the movement from the first position to the second position, the actuator 20 causes the driver 28 to engage the trailing edge 62 of the ratchet tooth 32 of the wheel 30. As the actuator 20 and driver 28 move down the ratchet-toothed wheel 30 rotates.

The spindle of the rotary gear moves the counter tape 44 revealing the next integer. The counter tape 44 is held taut by the action of the split hub 70 on which is mounted the stock bobbin 68.

The pawl 60 radially outwardly deforms to allow the wheel 30 to rotate by one tooth 32. The at least two teeth 64,66 of pawl 60 may be inherently resilient to allow the required radially outward deformation and return. Alternatively or in addition, the pawl 60 may be mounted on a resilient support capable of radially outward deformation, for example the resilient support may be a resilient flange incorporated in to the chassis of the dose counter 18.

The driver 28 releases the ratchet-toothed wheel 30 after it has engaged with the pawl 60. On reset of the inhaler, the canister 6 is allowed to return to its initial (first) position. The compression spring 24 pushes the actuator 20 to follow the canister. The driver 28 on the actuator 20 flexes to pass over the teeth of the ratchet-toothed wheel 30 as the actuator 20 moves from the first to the second position.

The tooth of the at least two teeth 64,66 which has engaged tooth 32 of the wheel 30 prevents the rotary gear from rotating backwards.

The counter mechanism of the type described with reference to WO 98/28033 and in accordance with the present invention must rotate the wheel 30 of the rotary gear by exactly one tooth spacing each time the actuator is depressed. By tooth spacing is meant one tooth pitch, i.e. the radial

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distance between the same notional point two adjacent teeth **32** on the ratchet-toothed wheel **30**. The stroke available for indexing the rotary gear is equal to the full stroke of the actuator **2**. Where the metered-dose inhaler is a pressurised inhaler, the stroke available for counting is equal to the full stroke of the medicament canister **6**. However, there are three movements (or “journeys”) that must be completed within this total distance for indexing of the dose counter to occur. The three journeys are shown schematically in FIG. 7.

FIG. 7 shows a graphical representation the amount of canister travel and the excess stroke available before the three critical journeys must occur. Firstly, the canister travel must close the start gap which is the sum of the tolerances of the manufactured components in the vertical direction. Secondly, the stroke must take up any lost motion, such as in pivot play, flexing of the pawl and arc motion of the drive pawl. Thirdly, is the so-called “stroke to count”, which is the journey which leads to indexing of the rotary gear by one tooth spacing.

The stroke available for counting will clearly depend on the type of metered-dose inhaler used. By way of example, a suitable inhaler is the pressurised metered-dosed inhaler EasiBreathe® which uses a Qvar® canister. The canister stroke in this inhaler was measured as 3.04 ± 0.255 mm. This tolerance represents ± 3 standard deviations so that 99.7% of all canister strokes will lie within these limits. The measurements were taken from force versus displacement profiles for Qvar® canisters. One hundred and fifty canisters were measured at the start, middle and end of life giving a total of 450 stroke measurements.

The start gap is the tolerance stack in the vertical direction and includes a first distance between the part of the driver **28** which engages the wheel **30** and the appropriate ratchet tooth **32** of the wheel **30** of the rotary gear, and a second distance between the top of the actuator **20** and the canister **6**. The tolerance in the vertical direction was found to be ± 0.47 mm. The nominal start gap for the EasiBreathe® inhaler is set at 0.85 mm and hence the start gap with tolerances is 0.85 ± 0.47 mm.

Thus, since the start gap is 0.85 ± 0.47 mm the maximum start gap (mean plus 3 standard deviations) is 1.32 mm (0.85 ± 0.47). When such a start gap occurs, a short-stroking canister (for example, 2.79 mm) will not rotate the wheel **30** of the rotary gear by a full tooth spacing. This will lead to failure of the dose counter. However, the provision of a first and second ratchet tooth **64,66** in the pawl **60** allows the ratchet tooth **32** of the wheel **30** of the rotary gear to rest on the second tooth **66**. In the present embodiment, the second tooth **66** is 0.60 mm away from the first tooth **64**. Thus, for the next actuation, the start gap is reduced to 0.72 mm ($1.32 - 0.60$). The stroke is therefore sufficient to rotate the wheel **30** a full index starting from this point. The step-wise rotation of the wheel **30** then continues with all subsequent actuations starting and finishing with the ratchet teeth **32** of the wheel **30** of the rotary gear engaged with the second tooth **66** of the pawl **60**.

FIG. 8 shows a more detailed view of the wheel **30** of the rotary gear, the driver **28** and the pawl **60** to prevent reverse rotation of the rotary gear. In FIG. 8(a) the ratchet tooth **32a** of the wheel **30** is engaged with the first ratchet tooth **64** of the pawl. In FIG. 8(b) the same tooth **32a** of the wheel **30** is engaged with the second ratchet tooth **66** of the pawl **60**. It may be seen that the start gap is reduced in the arrangement shown in FIG. 8(b) in comparison with the same distance in FIG. 8(a). The second tooth **66** of the pawl **60** therefore allows the first distance S of the start gap (the between the part of the driver **28** which engages the wheel **30** and the appropriate

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ratchet tooth **32** of the wheel **30**) to be reduced thereby accommodating a greater tolerance in the canister stroke.

As explained hereinabove, the first and second teeth **64,66** provide different starting positions for the wheel **30** of the rotary gear to accommodate different tolerance levels in the components of the inhaler. The teeth **64,66** are therefore separated radially with respect to the wheel **30**. The spacing will clearly depend on the precise nature of the components used in the inhaler and hence it would be inappropriate to provide a precise numerical value. It is clear from the mechanism, however, that the radial spacing will be less than the radial distance between adjacent teeth **32** on the wheel **30** of the rotary gear.

In the embodiments shown herein, the dose counter **18** of the present invention incorporates a pawl **60** having two teeth **64,66** and only two teeth, i.e. the pawl **60** consists essentially of two teeth **64,66**. However, additional teeth could be incorporated to provide additional precision to the start position of the wheel **30** and thus additional precision in the first distance S. For example, the pawl may have 2-6, preferably two, three or four teeth, more preferably two or three and most preferably two teeth.

In a particularly preferred embodiment of the present invention, the dose counter is adapted for a canister stroke of 3.041 ± 0.256 mm: the wheel of the rotary gear has a radius of 2.80 ± 0.05 mm defined as the distance from the centre of the wheel to the tip of the teeth and 11 ratchet teeth around its periphery; and the pawl comprises two ratchet teeth only which have a radial spacing of 0.6 mm. In this embodiment, the total stroke to guarantee a count is 2.372 ± 0.115 mm. The probability of failure to count or resent due to component dimension variations (manufacturing tolerances) is less than 1 in 10 million.

The present invention further provides a metered dose inhaler **72** as shown in FIG. 9. The inhaler comprises a medicament canister **6**, an actuator body **74** for receiving the canister **6** and having a medicament delivery outlet, and the dose counter as described herein. The inhaler has a window **76** for viewing the integers on the tape **44**. In a preferred embodiment the actuator body **74** comprises a sump and preferably a smooth rounded sump. Typically, a rounded sump is understood to have a substantially cylindrical upper portion and a substantially hemi-spherical lower portion. Typically, smooth is understood to mean that the surface is sufficiently free of surface protrusions to the extent that during normal use medicament will not substantially adhere thereto.

In one embodiment of the invention the vessel contains a medicament in the form of an aerosol. Alternatively in another embodiment of the invention the vessel contains a medicament in the form of a dry powder.

The medicament may be any medicament that is suitable to be delivered to a patient via a metered-dose inhaler. In particular medicaments for the treatment of a wide variety of respiratory disorders are delivered in this manner including anti-allergic agents (e.g. cromoglycate, ketotifen and nedocromil), anti-inflammatory steroids (e.g. beclomethasone dipropionate, fluticasone, budesonide, flunisolide, ciclesonide, triamcinolone acetonide and mometasone furoate); bronchodilators such as: β_2 -agonists (e.g. fenoterol, formoterol, pirbuterol, reproterol, salbutamol, salmeterol and terbutaline), non-selective β -stimulants (e.g. isoprenaline), and xanthine bronchodilators (e.g. theophylline, aminophylline and choline theophyllinate); and anticholinergic agents (e.g. ipratropium bromide, oxitropium bromide and tiotropium).

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A further aspect of the present invention provides the use of a pawl 60 comprising at least two ratchet teeth 64,66 for preventing miscounting in a dose counter of a metered dose inhaler 72. A still further aspect of the present invention provides the use of a pawl 60 comprising at least two ratchet teeth 64,66 for preventing undercounting in a counter of a metered dose inhaler 72.

In a preferred embodiment the counter comprises an actuator 20; a rotary gear; a driver 28 for driving the rotary gear in a step-wise fashion in response to displacement of the actuator 20, the rotary gear comprising a wheel 30 mounted on a spindle 36 which wheel 30 having a plurality of ratchet teeth 32 around its periphery; and a display 44 coupled to the rotary gear, the display having a visible array of incrementing integers on a surface thereof indexable by a single integer in response to each step of the step-wise rotary motion of the rotary gear. Preferably, the pawl 60 prevents reverse rotation of the rotary gear.

Although the invention herein has been described with reference to particular embodiments, it is to be understood that these embodiments are merely illustrative of the principles and applications of the present invention. It is therefore to be understood that numerous modifications may be made to the illustrative embodiments and that other arrangements may be devised without departing from the spirit and scope of the present invention as defined by the appended claims.

The invention claimed is:

1. A dose counter for a metered-dose inhaler, the counter comprising: an actuator; a rotary gear; a driver for driving the rotary gear in a step-wise fashion in response to displacement of the actuator, the rotary gear comprising a wheel mounted on a spindle which wheel having a plurality of ratchet teeth around its periphery; a pawl to prevent reverse rotation of the rotary gear; and a display coupled to the rotary gear, the display having a visible array of incrementing integers on a surface thereof indexable by a single integer in response to each step of the step-wise rotary motion of the rotary gear; wherein the pawl comprises at least two ratchet teeth each for engaging with the ratchet teeth of the wheel to prevent reverse rotation of the rotary gear, the at least two ratchet teeth being radially spaced such that one of the at least two ratchet teeth of the pawl engages with the ratchet teeth of the wheel following each step of the step-wise rotary motion of the rotary gear.

2. A dose counter as claimed in claim 1, wherein the pawl comprises two ratchet teeth and no more.

3. A dose counter as claimed in claim 1, wherein the pawl is mounted on a resilient support.

4. A dose counter as claimed in claim 3, wherein the resilient support is a resilient flange incorporated into the body of the dose counter.

5. A dose counter as claimed in claim 1, further comprising a control surface to regulate the position of engagement and disengagement between the driver and the wheel.

6. A dose counter as claimed in claim 1, wherein the actuator is operable by linear displacement from a first position to a second position and back to the first position and wherein movement of the rotary gear occurs either during the displacement of the actuator from the first position to the second position or during the displacement of the actuator from the second position to the first position.

7. A dose counter as claimed in claim 1, wherein the actuator comprises a spring-loaded plunger, the plunger being depressible against a return force of a spring of the spring-loaded plunger when the actuator is caused to deliver a dose of medicament.

8. A dose counter as claimed in claim 1, wherein the driver comprises a ratchet drive pawl.

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9. A dose counter as claimed in claim 8, wherein the ratchet drive pawl is in the form of a straddle drive in which an element that engages the ratchet teeth of the wheel is supported between a pair of spaced apart support arms.

10. A dose counter as claimed in claim 1, wherein the display is an elongate counter tape on which a dose count is printed or written.

11. A dose counter as claimed in claim 10, wherein the counter tape is located on an indexing spool and the dose counter further comprises a stock bobbin to receive the counter tape as the indexing spool is advanced in a step-wise fashion.

12. A dose counter as claimed in claim 1, wherein the actuator is adapted to engage with a rim of a medicament canister.

13. A dose counter as claimed in claim 1, wherein the wheel of the rotary gear has eight to fourteen ratchet teeth around a periphery of the rotary gear.

14. A dose counter as claimed in claim 13, wherein the wheel of the rotary gear has eleven ratchet teeth around its periphery.

15. A dose counter as claimed in claim 1, wherein the wheel of the rotary gear has a radius defined as the distance from the centre of the wheel to a tip of the teeth of 2.80 ± 0.05 mm and eleven ratchet teeth around its periphery, and the pawl comprises two ratchet teeth and no more which have a radial spacing of about 0.6 mm.

16. A metered dose inhaler comprising a medicament canister, an actuator body for receiving the canister and having a medicament delivery outlet, and the dose counter as claimed in claim 1.

17. A metered dose inhaler according to claim 16 wherein the actuator body comprises a smooth rounded sump.

18. The use of a dose counter for preventing miscounting in a metered dose inhaler, the dose counter comprising: an actuator; a rotary gear; a driver for driving the rotary gear in a step-wise fashion in response to displacement of the actuator, the rotary gear comprising a wheel mounted on a spindle which wheel having a plurality of ratchet teeth around its periphery; a pawl to prevent reverse rotation of the rotary gear; and a display coupled to the rotary gear, the display having a visible array of incrementing integers on a surface thereof indexable by a single integer in response to each step of the step-wise rotary motion of the rotary gear; wherein the pawl comprises at least two ratchet teeth each for engaging with the ratchet teeth of the wheel to prevent reverse rotation of the rotary gear, the at least two ratchet teeth being radially spaced such that one of the at least two ratchet teeth of the pawl engages with the ratchet teeth of the wheel following each step of the step-wise rotary motion of the rotary gear.

19. The use of a dose counter for preventing undercounting in a metered dose inhaler, the dose counter comprising: an actuator; a rotary gear; a driver for driving the rotary gear in a step-wise fashion in response to displacement of the actuator, the rotary gear comprising a wheel mounted on a spindle which wheel having a plurality of ratchet teeth around its periphery; a pawl to prevent reverse rotation of the rotary gear; and a display coupled to the rotary gear, the display having a visible array of incrementing integers on a surface thereof indexable by a single integer in response to each step of the step-wise rotary motion of the rotary gear; wherein the pawl comprises at least two ratchet teeth each for engaging with the ratchet teeth of the wheel to prevent reverse rotation of the rotary gear, the at least two ratchet teeth being radially spaced such that one of the at least two ratchet teeth of the pawl engages with the ratchet teeth of the wheel following each step of the step-wise rotary motion of the rotary gear.

* * * * *

EXHIBIT B

US008931476B2

(12) **United States Patent**
Kaar et al.

(10) **Patent No.:** **US 8,931,476 B2**
(45) **Date of Patent:** **Jan. 13, 2015**

(54) **INHALER**

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See application file for complete search history.

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PCT Pub. Date: **Dec. 16, 2010**

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(51) **Int. Cl.**

A61M 11/00 (2006.01)

A61M 15/00 (2006.01)

(52) **U.S. Cl.**

CPC **A61M 15/009** (2013.01); **A61M 15/0091** (2013.01); **A61M 15/0026** (2014.02)

USPC **128/200.23**; 128/200.12; 128/203.12

(58) **Field of Classification Search**

CPC A61M 15/009; A61M 15/0065; A61M 15/0091

USPC 128/200.23, 200.12, 200.14, 203.15,

Primary Examiner — Steven Douglas

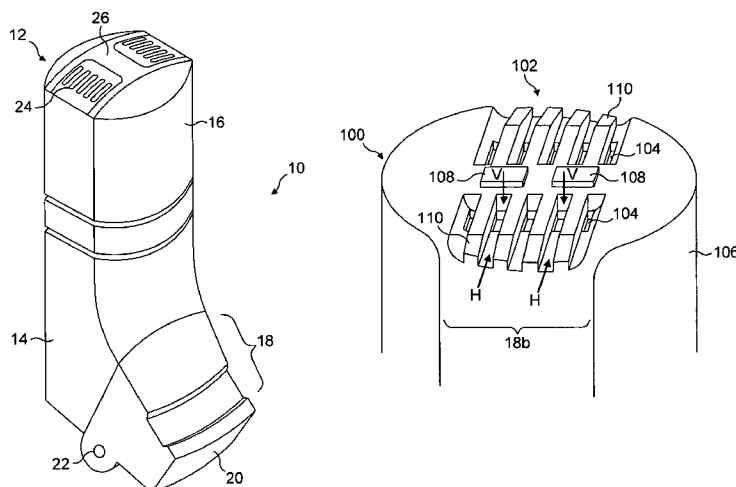
(74) *Attorney, Agent, or Firm* — RatnerPrestia

(57)

ABSTRACT

An inhaler, such as a breath-actuated metered-dose inhaler, for delivering medicament to a patient. The inhaler includes a housing for holding the medicament and having an air inlet and a medicament delivery port which together define an air flow path into which the medicament is dispensed. The air inlet includes an array of elongate apertures formed in the housing, the long sides of adjacent apertures facing each other. Each aperture is provided with a respective different opening in an outer surface of the housing. The opening of each aperture extends in two different planes such that, if at least a part of the opening is covered in one of the two different planes during inhalation by the patient, a void space is created between the cover and the aperture so as to provide an air flow path through the void space to the at least one aperture.

18 Claims, 2 Drawing Sheets



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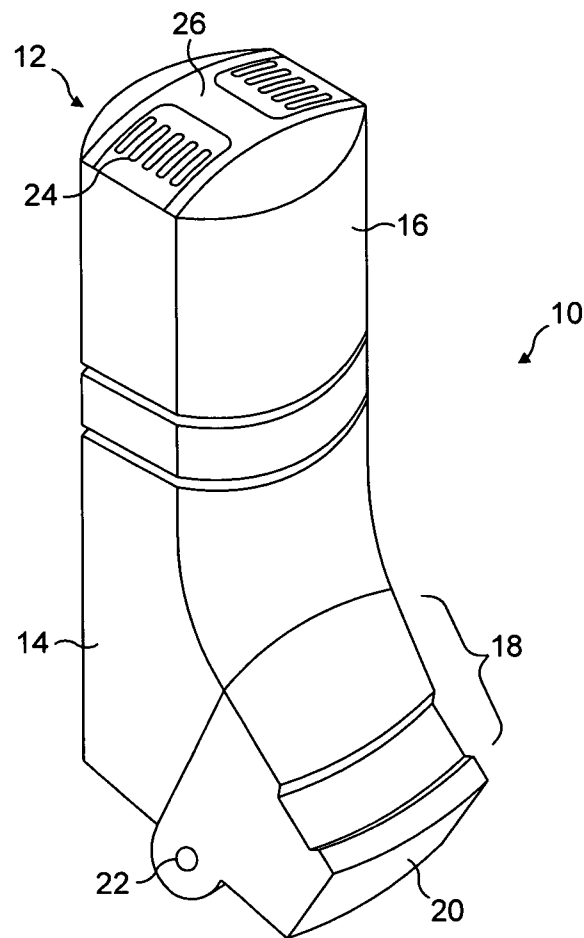


FIG. 1

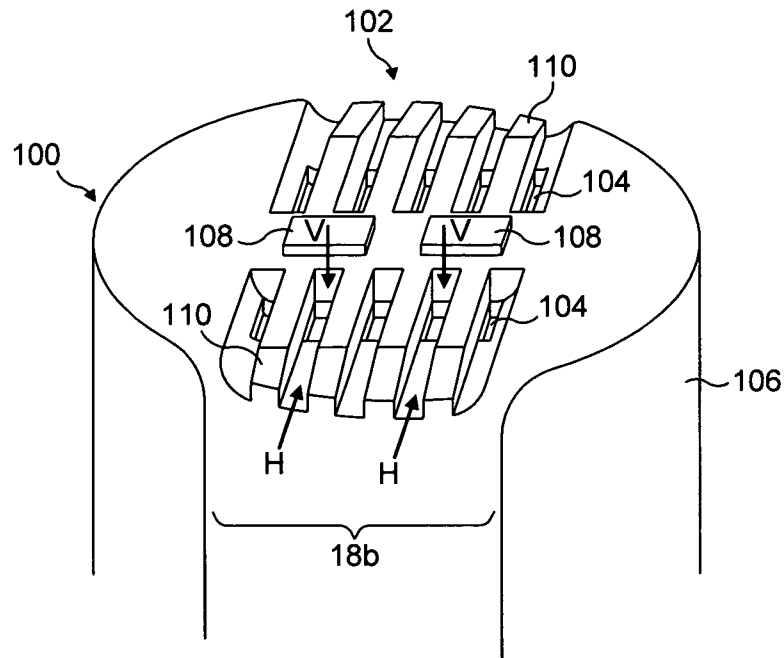


FIG. 2

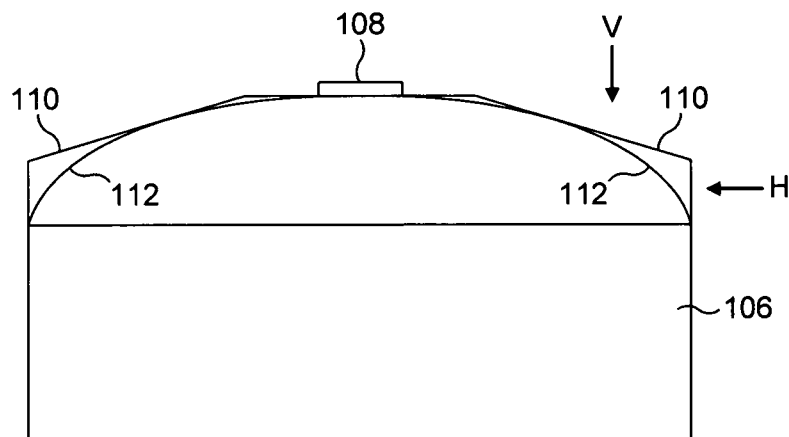


FIG. 3

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INHALERCROSS-REFERENCE TO RELATED
APPLICATIONS

This application is the U.S. national phase application of PCT International Application No. PCT/EP2010/003426, filed Jun. 8, 2010, which claims priority to U.S. Provisional Patent Application No. 61/185,380, filed Jun. 9, 2009, and Great Britain Patent Application No. 0910537.0, filed Jun. 18, 2009, the contents of such applications being incorporated by reference herein.

FIELD OF THE INVENTION

This invention relates to an inhaler for delivering medication to a patient, and more particularly to a metered-dose inhaler.

BACKGROUND TO THE INVENTION

Inhalers for delivering medicament to a patient by inhalation are known. Such devices include metered-dose inhalers (of both pressurised and dry-powder types). Metered-dose inhalers typically comprise a medicament-containing vessel and an actuator housing having a medicament delivery outlet in the form of a mouthpiece or nosepiece.

The medicament-containing vessel may be a pressurised canister containing a mixture of active medicament and propellant. Such canisters are usually formed from a deep-drawn aluminium cup having a crimped lid which carries a metering valve assembly. The metering valve assembly is provided with a protruding valve stem which, in use, is inserted as a tight push fit into a so-called stem block in the actuator housing.

Metered-dose inhalers may either be of the manually operable type or the breath-actuated type. For the manually operable type, the patient self-administers the medicament by manually pressing the closed end of the canister into the actuator housing to cause movement of the canister relative to its valve stem (which is fixed in the stem block of the actuator housing). This movement is sufficient to actuate the metering valve assembly of the canister, resulting in the pressurised contents of a metering chamber being vented through the stem, through the stem block and its exit jet and orifice, and causing the medicament to exit the mouthpiece or nosepiece as an aerosol mist. Simultaneously with this action, the patient inhales through the nosepiece or mouthpiece, entraining the aerosol mist in the inhaled stream of air. The patient then releases the depression force on the canister which, under the action of an internal valve spring, moves upward with respect to the valve stem, returning to its resting position.

A more recent development is the so-called breath-actuated metered-dose inhaler, which serves to automatically displace the canister relative to its valve stem and release the contents of the canister's metering chamber in response to a patient's inspiration. The general purpose of such inhalers is to alleviate difficulties in coordinating actuation of the metering valve assembly with the patient's inspiration, and to provide for a maximal amount of medication to be drawn into the patient's lungs. A breath-actuated metered-dose inhaler is disclosed in WO 01/93933 A2.

The actuator housing is generally regarded as an integral part of the medicament delivery system, since the design of the housing can greatly affect the form of the medicament generated for inhalation by the patient. The actuator housing of a metered-dose inhaler typically includes an air inlet means

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for producing an air flow through the actuator housing into which the medicament is released.

Further, for breath-actuated inhalers, the air flow through the actuator housing typically operates or at least influences in some way the breath-actuated mechanism. Consequently, the actuator housing of such inhalers comprises air inlets designed to allow airflow through the housing. However, such air inlets exhibit the problem that they can be covered or occluded by the patient's hand or finger during use, thereby preventing or influencing the airflow through the actuator housing, with the result that the breath-actuated mechanism may malfunction. This problem is often exacerbated by the fact that the air inlets are provided on the actuator housing at positions which are convenient for handling the inhaler during use by the patient.

Thus, there is a need in the art to provide improved airflow configurations for inhalers that are less susceptible to being occluded or blocked by the patient during use, while at the same time allowing for convenient and comfortable operation by the patient.

SUMMARY OF THE INVENTION

According to the invention, there is provided an inhaler for delivering medicament to a patient, the inhaler comprising a housing for holding the medicament and having an air inlet means and a medicament delivery port which together define an air flow path into which the medicament is dispensed,

wherein the air inlet means comprises an array of elongate apertures formed in the housing, the long sides of adjacent apertures facing each other, and each aperture being provided with a respective different opening in an outer surface of the housing,

and wherein the opening of each aperture extends in two different planes such that, if at least a part of the opening is covered in one of the two different planes during inhalation by the patient, a void space is created between the cover and the aperture so as to provide an air flow path through the void space to the at least one aperture.

The inventors have found that the provision of multiple elongate apertures having respective different openings, each extending in two different planes, minimises the risk of the air inlet means becoming blocked. By different openings, it is meant that the opening of each aperture is defined, at least in part, by surfaces which are unique to that opening.

Embodiments of the invention may therefore prevent the air inlet means from being blocked by the patient during use, particularly by the patient's finger or thumb which each comprise soft tissue and can conform to different surface relief. By providing void spaces between the patient and the apertures when the patient covers the air inlet means, a substantial air flow path can be maintained which enables air to flow through the air inlet means despite the air inlet means being covered by the patient.

Embodiments may be particularly advantageous for use in conjunction with metered-dose inhalers, and particularly breath-actuated inhalers of this type containing a pressurised aerosol canister.

The invention may be applied to known inhalers with only minimal design changes, thereby reducing the potential for patient confusion, and avoiding large tooling costs that would be associated with more significant design changes.

The apertures of the air inlet means may be arranged to be parallel to one another. In this way, it may be possible to maximise the air flow through an air inlet means having a predetermined cross-sectional area. Raised, elongate forma-

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tions having the form of ribs may be provided between adjacent apertures to define the different openings of the apertures.

The apertures may have a length in the range 2 mm to 20 mm, preferably in the range 4 mm to 12 mm. The apertures may have a width in the range 0.5 mm to 2 mm, preferably about 1 mm. The distance between adjacent apertures may be the same as the width of the apertures. The raised surface formations provided between adjacent apertures may have a height in the range 0.5 mm to 5 mm, preferably 1 mm to 3 mm.

In embodiments, each aperture is in effect provided in a respective different recess in the outer surface of the housing, which recess defines the opening of the aperture. The area of the opening of each aperture (in the outer surface of the housing) may be larger than an area of the aperture in the inner surface of the housing, for example the recess may surround the aperture. In general, however, it is preferred that at least one dimension of the recess is the same as, or similar to, the corresponding dimension of the aperture, in order to minimise the risk of the air inlet means becoming blocked.

As mentioned above, it is an essential feature of the invention that the opening of each aperture extends in two different planes, that is to say the opening defines some curvature or an edge between angled planes. In preferred embodiments, the opening of each aperture extends in different planes defining an angle of at least 45 degrees, and more preferably at least 60 degrees, and most preferably at least 80 degrees.

The housing may comprise an elongate body, which body may be unitary or multi-part. The air inlet means may conveniently be provided at an end of the elongate body opposite to an end at which the medicament delivery port is provided. In this case, the air inlet means may comprise a pair of the arrays of elongate apertures arranged at opposite sides of the end face of the elongate body, with a raised, elongate surface formation provided between the arrays.

The inhaler may be a metered-dose inhaler, particularly a breath-actuated metered-dose inhaler. The housing may be adapted for receiving a medicament-containing pressurised canister.

BRIEF DESCRIPTION OF THE DRAWINGS

An embodiment of the invention will now be described, by way of example only, with reference to the accompanying diagrams, in which:

FIG. 1 shows an inhaler having an air inlet means according to the prior art document WO 01/93933 A2;

FIG. 2 is an enlarged view of an inhaler having an air inlet means according to an embodiment of the invention; and

FIG. 3 is side view of the inhaler shown in FIG. 2.

DETAILED DESCRIPTION

The invention provides an inhaler, such as a breath-actuated pressurised metered-dose inhaler, for delivering medicament to a patient. The inhaler comprises a housing for holding the medicament, and having an air inlet means and a medicament delivery port which together define an air flow path into which the medicament is dispensed. The air inlet means comprises an array of elongate apertures formed in the housing, the long sides of adjacent apertures facing each other. Each aperture is provided with a respective different opening in an outer surface of the housing. The opening of each aperture extends in two different planes such that, if at least a part of the opening is covered in one of the two different planes during inhalation by the patient, a void space is created

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between the cover and the aperture so as to provide an air flow path through the void space to the at least one aperture.

Referring to FIG. 1, there is shown a breath-actuated pressurised metered-dose inhaler 10 having an air inlet means 12 according to the prior art document WO 01/93933 A2 (the entire disclosure of which is incorporated herein by reference). A detailed explanation of the principle of operation of the inhaler 10 is not essential for understanding the invention, but a brief explanation will be provided by way of background information.

The inhaler 10 comprises a main body 14 and an end cap 16 which together define an elongate actuator housing. The main body 14, which is generally cylindrical in cross-section, is provided with a laterally extending mouthpiece 18 at one end and at the other end is adapted to receive a portion of a cylindrical medicament-containing pressurised canister. A stem block (not shown) is provided within the main body 14 for receiving the valve stem of the canister, and includes an exit jet and orifice communicating with the mouthpiece 18.

The end cap 16, which is also generally cylindrical in cross-section, is provided with the air inlet means 12 at one end and at the other end is adapted to receive the remaining portion of the canister. The main body 14 and end cap 16 are connected together by a threaded coupling. Components of the breath-actuated mechanism (not shown) are contained within both the main body 14 and the end cap 16.

The breath-actuated mechanism and canister contained within the housing 14, 16 provide one or more air pathways such that air may pass from the air inlet means 12 to the mouthpiece 18 through the inside of the housing 14, 16.

The mouthpiece 18 is provided with a dust cap 20 rotatable about an axis 22 between a first (closed) position (as shown in FIG. 1) and a second (open) position. In use, the patient rotates the dust cap 20 to its open position and inserts the exposed mouthpiece 18 into their mouth. On inhalation by the patient through the mouthpiece 18, a pressure differential in the housing 14, 16 causes the breath-actuated mechanism to automatically displace the canister relative to its valve stem. Medicament contained within the metering chamber of the canister is accordingly released in response to the patient's inspiration.

During the patient's inspiration, air flows from the air inlet means 12, through the housing 14, 16, to the mouthpiece 18, and therefore to the patient. The medicament released from the metering chamber of the canister is entrained in this airflow.

After inhalation of the dose of medicament by the patient, the dust cap 22 is returned to its closed position, and this causes the breath-activated mechanism and the aerosol canister to reset to a rest position ready for subsequent use.

The air inlet means 12 of the inhaler 10 shown in FIG. 1 comprises a plurality of elongate apertures 24 formed in the end face of the end cap 16. The apertures 24 are arranged in a pair of arrays provided on opposite sides of the end face. Although there is a limited amount of three-dimensionality 26 provided between the arrays, the openings of adjacent apertures 24 in each of the arrays define a flat surface. Consequently, in use of the inhaler, it is a problem that the apertures 24 can become blocked by the finger or thumb of the patient, which may lead to a malfunction of the breath-actuated mechanism and/or incomplete or ineffective delivery of the medicament to the patient.

Referring now to FIGS. 2 and 3, there is shown enlarged view of an inhaler 100 having an air inlet means 102 according to an embodiment of the invention. With the exception of its air inlet means 102, the inhaler 100 according to the invention has the same structure and use as the known inhaler

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10 shown in FIG. 1. A detailed description of the individual components of the inhaler 100, other than the end cap having the air intake means 102, will accordingly be omitted. Similarly, a detailed description of the use of the inhaler 100 will also be omitted.

The air inlet means 102 of the inhaler 100 comprises a plurality of parallel, elongate apertures 104 having an approximately rectangular shape. The apertures 104 are formed in the end face of the end cap 106. The apertures 104 are arranged in two distinct arrays provided on opposite sides of the end face, each array comprising five apertures 104 whose long sides face one another. Short sides of the apertures 104 in one of the arrays face short sides of the apertures 104 in the other of the arrays, and are separated by a pair of elongate surface protrusions 108 which extend in a direction perpendicular to the length direction of the apertures 104.

Each of the apertures 104 is effectively recessed in the surface of the end cap 106, and the recess defines an opening of the aperture 104. The recesses are defined by raised, elongate surface protrusions in the form of moulded ribs 110 arranged between the long sides of adjacent apertures 104. Each recess is open at one end, with a corresponding end of each rib 110 being chamfered. As such, the opening of each aperture 104 extends in two substantially perpendicular planes: a horizontal plane corresponding to the "top" portion of the opening and a vertical plane corresponding to the "side" portion of the opening.

The apertures 104 have lengths which vary from 5 mm to 7 mm, and a width of 1 mm. A spacing between apertures 104 is 1.2 mm, and the elongate ribs 104 filling these spaces have a height of 2.5 mm.

In use of the inhaler 100, if the patient covers at least a part of the openings of the apertures 104 in one of the two different planes, for example with their finger or thumb, then void spaces are created between the patient and the apertures 104 so as to provide an air flow path through the void spaces to the apertures 104, thereby preventing the apertures 104 from being occluded or blocked by the patient.

In other words, if the air inlet means 102 is covered by a surface extending in the horizontal plane which prevents vertical air flow (as illustrated by the arrows labelled "V" in FIGS. 2 and 3) into the apertures 104, for example, the configuration of the air inlet means 102 is such that the openings of the apertures 104 extend at least partially in the vertical plane enabling horizontal air flow (as illustrated by the arrows labelled "H" in FIGS. 2 and 3) into the apertures 104. Conversely, if the air inlet means 102 is covered by a surface extending in the vertical plane which prevents horizontal air flow (as illustrated by the arrows labelled "H") into the apertures 104, the configuration of the air inlet means 102 is such that the openings of the holes 24 extend in the horizontal to plane enabling vertical air flow (as illustrated by the arrows labelled "V") into the apertures 104.

With specific reference to FIG. 3, it can be seen that the elongate ribs 110 which define the openings of the apertures 104 stand proud of the surrounding surface 112 of the end cap 106. The elongate ribs 110 thus ensure a void space can be maintained between the patient's finger or thumb and the apertures 104.

A specific embodiment has been described herein for purpose of illustration. Various modifications will be apparent to a person skilled in the art and may be made without departing from the scope of the invention.

For example, although the embodiment described above is implemented as breath-actuated pressurised metered-dose inhaler, it will be understood that alternative embodiments may more generally comprise an inhaler for delivering medication to a patient by inhalation, wherein restriction or prevention of blockage of air inlets by the patient is desirable. Such prevention of blockage may, for example, be desirable

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in dry-powder inhalers in which a source of air is required for effective atomization of the medicament.

In the embodiment described above, the air inlet means is arranged in an end face of the end cap. In alternative embodiments the air inlet means may be provided elsewhere, such as in the end face of the main body, adjacent to the mouthpiece.

Components of an inhaler according to the invention will typically be moulded plastics components. Such components can conveniently be provided with the surface features of the invention.

In embodiments the inhaler comprises a medicament-containing pressurised canister containing a medicament and a propellant.

Typically, the medicament is selected from the group consisting of anti-inflammatory agents, anti-cholinergic agents, β_2 -adrenoreceptor agonists, anti-infective agents, anti-histamines and combinations thereof.

Suitable anti-inflammatory agents include corticosteroids and NSAIDs. Suitable corticosteroids which may be used include those oral and inhaled corticosteroids and their prodrugs which have anti-inflammatory activity. Examples include methyl prednisolone, prednisolone, dexamethasone, fluticasone propionate, 6a,9a-difluoro-17a-[(2-furanylcarbonyl)oxy]-11-hydroxy-16a-methyl-3-oxo-androsta-1,4-diene-17-carbothioic acid S-fluoromethyl ester, 6a,9a-difluoro-11-hydroxy-16a-methyl-3-oxo-17a-propionyloxy-androsta-1,4-diene-17p-carbothioic acid S-(2-oxo-tetrahydro-furan-3S-yi) ester, beclomethasone esters (e.g. the 17-propionate ester or the 17,21-dipropionate ester), budesonide, flunisolide, mometasone esters (e.g. the furoate ester), triamcinolone acetonide, rofleponide, ciclesonide, butixocort propionate, RPR-106541, and ST-126. Preferred corticosteroids include fluticasone propionate, 6a,9c-difluoro-11-hydroxy-16a-methyl-17a-[(4-methyl-1,3-thiazole-5-carbonyl)oxy]-3-oxo-androsta-1,4-diene-17,8-carbothioic acid S-fluoromethyl ester and 6a,9a-difluoro-17a-[(2-furanylcarbonyl)oxy]-11-hydroxy-16a-methyl-3-oxo-androsta-1,4-diene-17-carbothioic acid S-fluoromethyl ester, more preferably 6a,9a-difluoro-17a-[(2-furanylcarbonyl)oxy]-11-hydroxy-16a-methyl-3-oxo-androsta-1,4-diene-17-carbothioic acid S-fluoromethyl ester.

Suitable NSAIDs include sodium chromoglycate, nedocromil sodium, phosphodiesterase (PDE) inhibitors (e.g. theophylline, PDE4 inhibitors or mixed PDE3/PDE4 inhibitors), leukotriene antagonists, inhibitors of leukotriene synthesis, iNOS inhibitors, tryptase and elastase inhibitors, beta-2 integrin antagonists and adenosine receptor agonists or antagonists (e.g. adenosine 2a agonists), cytokine antagonists (e.g. chemokine antagonists) or inhibitors of cytokine synthesis.

Suitable other β_2 -adrenoreceptor agonists include salmeterol (e.g. as the xinofoate), salbutamol (e.g. as the sulphate or the free base), formoterol (e.g. as the fumarate), fenoterol or terbutaline and salts thereof.

Suitable anticholinergic agents are those compounds that act as antagonists at the muscarinic receptor, in particular those compounds, which are antagonists of the M1 and M2 receptors. Compounds include the alkaloid of the belladonna plants as illustrated by the likes of atropine, scopolamine, homatropine, hyoscyamine; these compounds are normally administered as a salt, being tertiary amines.

Particularly suitable anticholinergics include ipratropium (e.g. as the bromide), sold under the name Atrovent, oxitropium (e.g. as the bromide) and tiotropium (e.g. as the bromide) (CAS-139404-48-1). Also of interest are: methantheline (CAS-53-46-3), propantheline bromide (CAS-50-34-9), anisotropine methyl bromide or Valpin 50 (CAS-80-50-2), clidinium bromide (Quarzan, CAS-3485-62-9), copyrrolate (Robinul), isopropamide iodide (CAS-71-81-8), mepenzolate bromide (U.S. Pat. No. 2,918,408), tridihex-

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ethyl chloride (Pathilone, CAS-4310-35-4), and hexocyclium methylsulfate (Tral, CAS-1,5-63-9). See also cyclopentolate hydrochloride (CAS-5870-29-1), tropicamide (CAS-1508-75-4), trihexyphenidyl hydrochloride (CAS-144-11-6), pirenzepine (CAS-29868-97-1), telenzepine (CAS-80880-90-9), AF-DX 116, or methoctramine, and the compounds disclosed in WO01/04118.

Suitable antihistamines (also referred to as H1-receptor antagonists) include any one or more of the numerous antagonists known which inhibit H1-receptors, and are safe for human use. All are reversible, competitive inhibitors of the interaction of histamine with H1-receptors. Examples include ethanolamines, ethylenediamines, and alkylamines. In addition, other first generation antihistamines include those which can be characterized as based on piperizine and phenothiazines. Second generation antagonists, which are non-sedating, have a similar structure-activity relationship in that they retain the core ethylene group (the alkylamines) or mimic the tertiary amine group with piperizine or piperidine. Exemplary antagonists are as follows:

Ethanolamines: carbinoxamine maleate, clemastine fumarate, diphenylhydramine hydrochloride, and dimenhydrinate.

Ethylenediamines: pyrilamine amleate, tripeleannamine HCl, and tripeleannamine citrate.

Alkylamines: chlorpheniramine and its salts such as the maleate salt, and acrivastine.

Piperazines: hydroxyzine HCl, hydroxyzine pamoate, cyclizine HCl, cyclizine lactate, meclizine HCl, and cetirizine HCl.

Piperidines: Astemizole, levocabastine HCl, loratadine or its descarboethoxy analogue, and terfenadine and fexofenadine hydrochloride or another pharmaceutical acceptable salt.

Azelastine hydrochloride is yet another H1 receptor antagonist which may be used in combination with a PDE4 inhibitor.

Particularly suitable anti-histamines include methapyrilene and loratadine.

Preferably the medicament is presented in a formulation comprising a propellant and preferably a solvent; other preferred ingredients include surfactants, including oleic acid. Preferred solvents include ethanol, glycerols and glycols.

Preferred propellants include hydrofluoroalkanes; in particular 1,1,1,2-tetrafluoroethane (HFA134a); 1,1,1,2,3,3,3-Heptafluoropropane (HFA227); or combinations thereof. Preferably, the medicament is suspended in the propellant. Alternatively the medicament is dissolved in the propellant. The medicament may also be part suspended and part dissolved in the propellant.

EXAMPLES

The following medicament formulations were used in the inhaler:

Example Formulation 1

Ingredient	Quantity/mg per ml
Beclomethasone dipropionate	1.00
Ethanol	94.80
HFA 134a	1090.20

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Example Formulation 2

Ingredient	Mass/mg
Salbutamol sulphate	0.1098
HFA 134a	27.8
Ethanol	3.6

The invention claimed is:

1. An inhaler for delivering medicament to a patient, the inhaler comprising a housing for holding the medicament and having an air inlet means and a medicament delivery port which together define an air flow path into which the medicament is dispensed,

wherein the air inlet means comprises an array of elongate apertures formed in the housing, wherein long sides of adjacent apertures face each other, and each aperture being provided with a respective different opening in an outer surface of the housing,

and wherein the opening of each aperture extends in two different planes such that, if at least a part of the opening is covered in one of two different planes during inhalation by the patient, a void space is created between a cover and the aperture so as to provide an air flow path through the void space to the at least one aperture, wherein a raised formation is provided in the outer surface of the housing between adjacent apertures to either limit or prevent a covered opening.

2. An inhaler according to claim 1, wherein the apertures are arranged to be parallel to one another.

3. An inhaler according to claim 1, wherein the raised formations are elongate raised formations.

4. An inhaler according to claim 1, wherein each aperture is provided in a respective different recess in the outer surface of the housing, which recess defines the opening of the aperture.

5. An inhaler according to claim 1, wherein the opening of each aperture extends in substantially perpendicular planes.

6. An inhaler according to claim 1, wherein the housing comprises an elongate body.

7. An inhaler according to claim 6, wherein the air inlet means is provided in an end face of the elongate body.

8. An inhaler according to claim 7, wherein the air inlet means comprises a pair of the arrays of elongate apertures arranged at opposite sides of the end face of the elongate body.

9. An inhaler according to claim 1, wherein the inhaler is a metered-dose inhaler.

10. An inhaler according to claim 1, wherein the inhaler is a breath-actuated metered-dose inhaler.

11. An inhaler according to claim 1, wherein the housing is adapted for receiving a medicament-containing pressurised canister.

12. An inhaler according to claim 11, wherein the inhaler comprises a medicament-containing pressurised canister containing a medicament and a propellant.

13. An inhaler according to claim 1, wherein the medicament is selected from the group consisting of anti-inflammatory agents, anti-cholinergic agents, β_2 -adrenoreceptor agonists, anti-infective agents, anti-histamines and combinations thereof.

14. An inhaler according to claim 12, wherein said medicament is dissolved in said propellant or said medicament is suspended in said propellant.

15. An inhaler according to claim 1, wherein the medicament is selected from the group consisting of salbutamol, formoterol, salmeterol, fluticasone, budesonide, beclomethasone, tiotropium, ipratropium and combinations thereof.

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16. An inhaler according to claim 7, wherein the medication delivery port is arranged at an opposite end of the elongated body to the end face.

17. A metered-dose inhaler for delivering medicament to a patient, the inhaler comprising a housing for holding the medicament and having an air inlet means and a medicament delivery port which together define an air flow path into which the medicament is dispensed,

wherein the housing comprises an elongate body and the air inlet means is provided in an end face of the elongate body,

wherein the air inlet means comprises an array of elongate apertures formed in the housing, long sides of adjacent apertures facing each other, and each aperture being provided with a respective different opening in an outer surface of the housing,

wherein each aperture is provided in a respective different recess in the outer surface of the housing, which recess defines the opening of the aperture,

and wherein the opening of each aperture in the outer surface of the housing extends in two different planes defining an angle of at least 45 degrees to each other, such that, if at least a part of the opening is covered in one of the two different planes during inhalation by the patient, a void space is created between the patient and the aperture so as to provide an air flow path through the void space to the at least one aperture.

18. An inhaler according to claim 17, wherein the medication delivery port is arranged at an opposite end of the elongate body to the end face.

* * * * *

UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

PATENT NO. : 8,931,476 B2
APPLICATION NO. : 13/377037
DATED : January 13, 2015
INVENTOR(S) : Simon Kaar et al.

Page 1 of 1

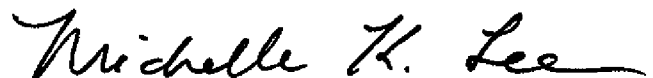
It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

In the Specification

At Column 2, line 50, “relief” should read --reliefs--

At Column 7, line 2, “CAS-1,5-63-9)” should read --CAS-115-63-9)--

Signed and Sealed this
Nineteenth Day of May, 2015

A handwritten signature in black ink, reading "Michelle K. Lee". The signature is fluid and cursive, with the first letters of each name being capitalized and prominent.

Michelle K. Lee
Director of the United States Patent and Trademark Office

EXHIBIT C

(12) **United States Patent**
Walsh et al.

(10) **Patent No.:** **US 10,022,509 B2**
(45) **Date of Patent:** **Jul. 17, 2018**

(54) **DOSE COUNTER FOR INHALER HAVING A BORE AND SHAFT ARRANGEMENT**

(71) Applicants: **IVAX PHARMACEUTICALS IRELAND**, Waterford (IE); **NORTON (WATERFORD) LIMITED**, Waterford (IE); **TEVA PHARMACEUTICALS IRELAND**, Waterford (IE)

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(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: **15/269,102**

(22) Filed: **Sep. 19, 2016**

(65) **Prior Publication Data**

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Related U.S. Application Data

(60) Continuation of application No. 14/699,578, filed on Apr. 29, 2015, which is a continuation of application (Continued)

(51) **Int. Cl.**
G06M 1/06 (2006.01)
A61M 11/00 (2006.01)
(Continued)

(52) **U.S. Cl.**
CPC **A61M 15/0078** (2014.02); **A61M 11/00** (2013.01); **A61M 15/009** (2013.01);
(Continued)

(58) **Field of Classification Search**
CPC . A61M 15/0078; A61M 11/00; A61M 15/009
(Continued)

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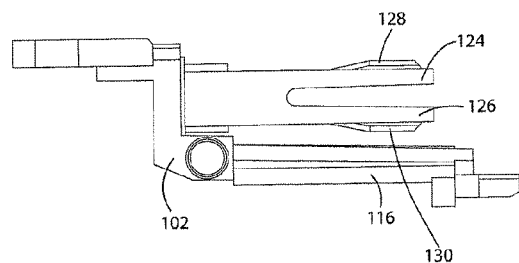
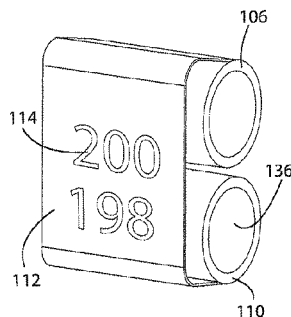
Primary Examiner — Daniel Hess

(74) *Attorney, Agent, or Firm* — Morgan, Lewis & Bockius, LLP

(57) **ABSTRACT**

A dose counter for an inhaler, the dose counter having a display tape arranged to be incrementally driven from a tape stock bobbin onto an incremental tape take-up drive shaft, the bobbin having an internal bore supported by and for rotation about a support shaft, at least one of the bore and support shaft having a protrusion which is resiliently biased into frictional engagement with the other of the bore and support shaft with longitudinally extending mutual frictional interaction.

16 Claims, 17 Drawing Sheets



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Related U.S. Application Data

- No. 14/103,353, filed on Dec. 11, 2013, now Pat. No. 9,526,850, which is a division of application No. 13/110,532, filed on May 18, 2011, now Pat. No. 8,978,966.
- (60) Provisional application No. 61/417,659, filed on Nov. 29, 2010, provisional application No. 61/345,763, filed on May 18, 2010.
- (51) **Int. Cl.**
A61M 15/00 (2006.01)
G06M 1/24 (2006.01)
- (52) **U.S. Cl.**
CPC *A61M 15/0025* (2014.02); *A61M 15/0026* (2014.02); *A61M 15/0065* (2013.01); *A61M 15/0071* (2014.02); *G06M 1/246* (2013.01); *A61M 2202/064* (2013.01); *A61M 2205/6063* (2013.01); *A61M 2207/00* (2013.01); *A61M 2207/10* (2013.01); *Y10T 29/49* (2015.01); *Y10T 29/49764* (2015.01); *Y10T 29/49826* (2015.01)
- (58) **Field of Classification Search**
USPC 235/8, 103, 87 R; 128/200.23, 200.1
See application file for complete search history.

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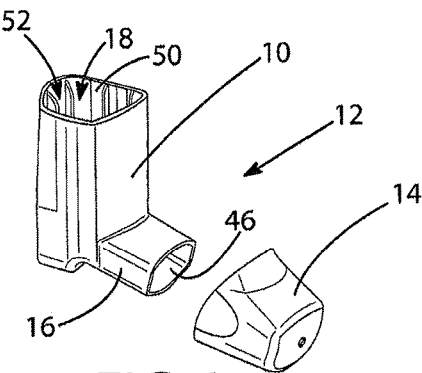


FIG. 1

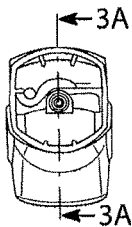


FIG. 2

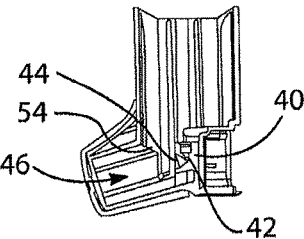


FIG. 3A

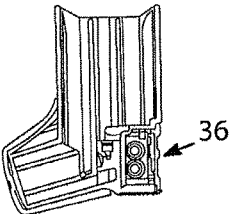


FIG. 3B

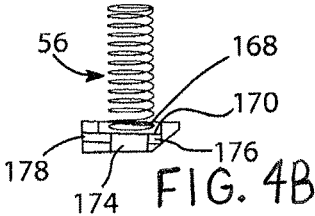


FIG. 4B

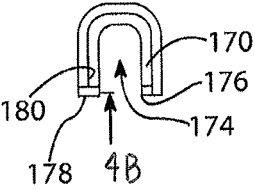


FIG. 4C

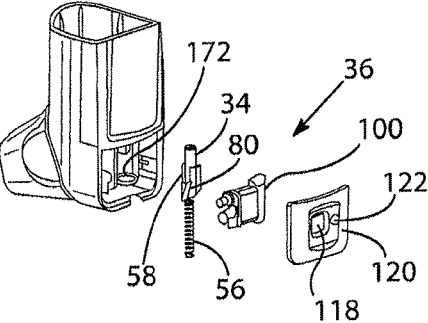


FIG. 4A

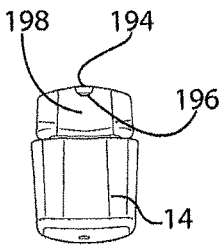


FIG. 5

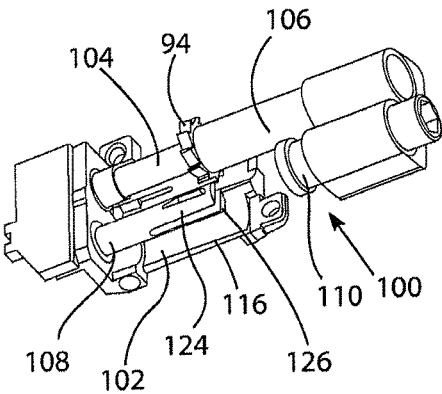


FIG. 6A

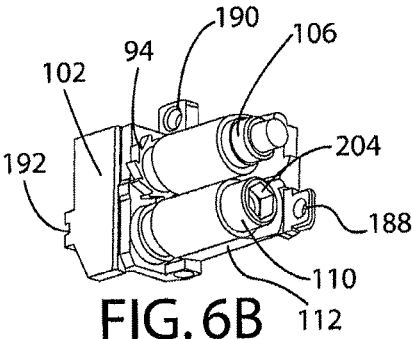


FIG. 6B

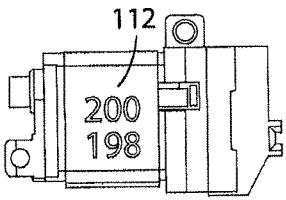


FIG. 6C

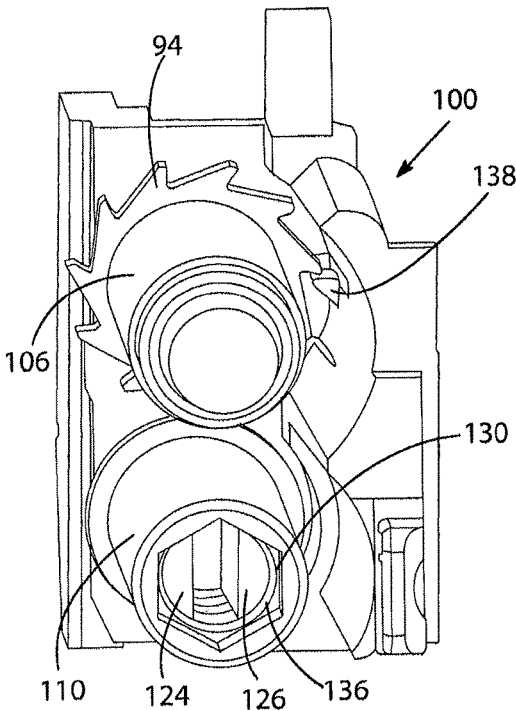


FIG. 6D

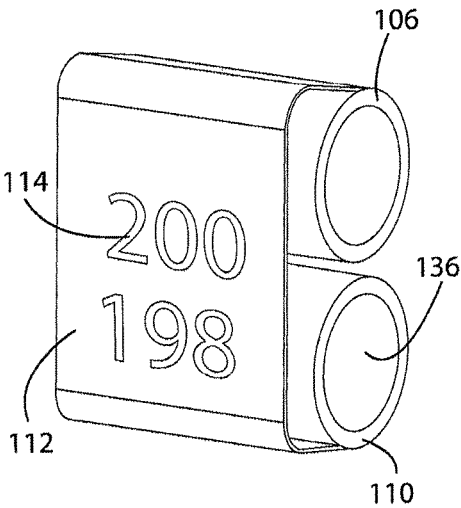


FIG. 6E

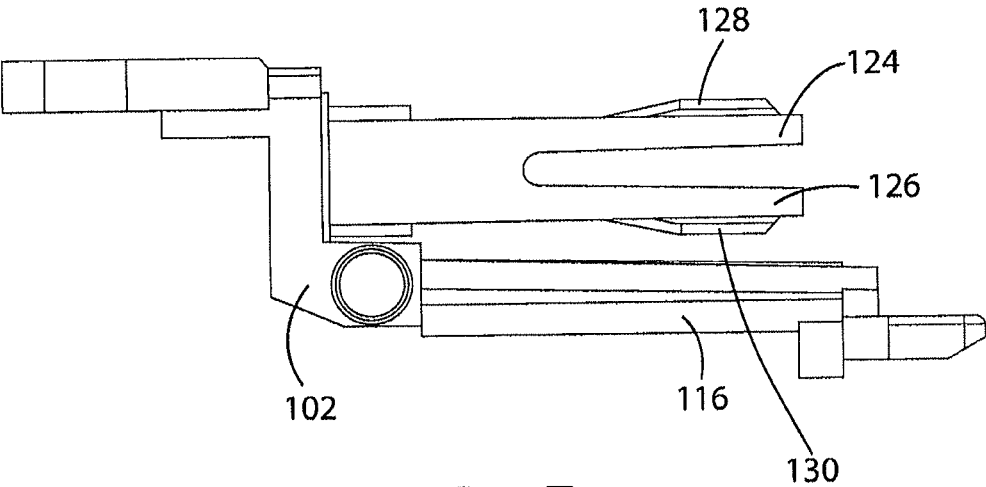


FIG. 6F

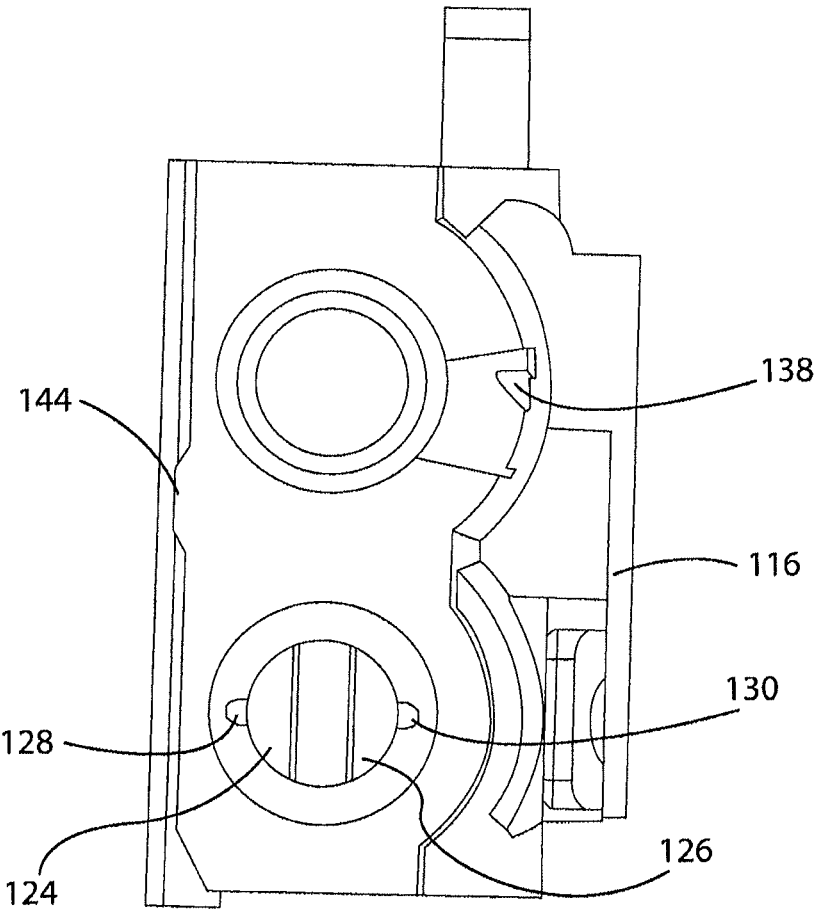


FIG. 6G

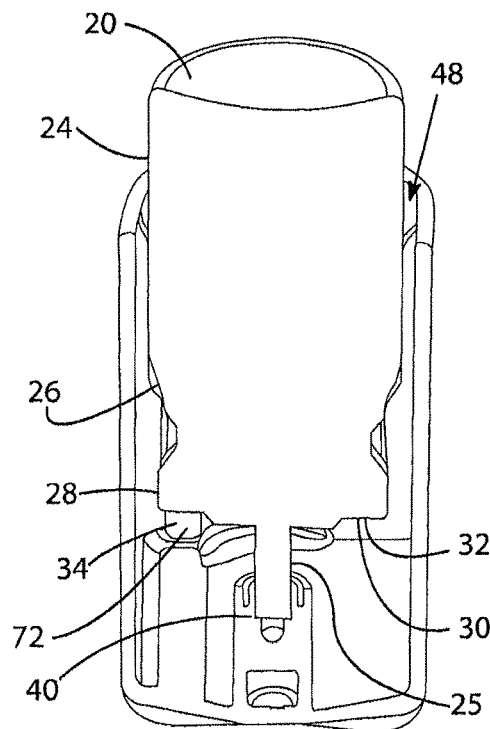


FIG. 7A

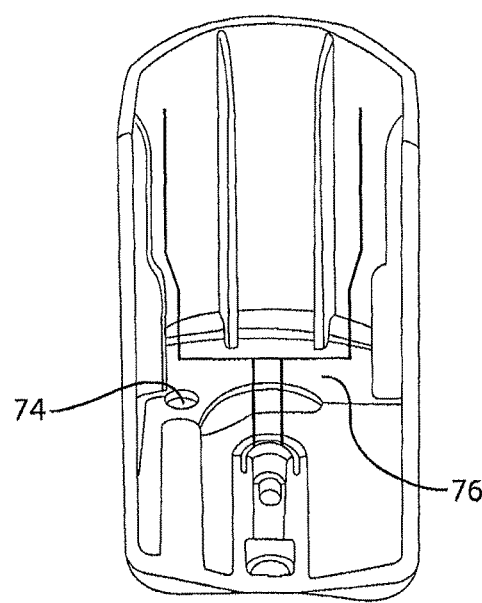


FIG. 7B

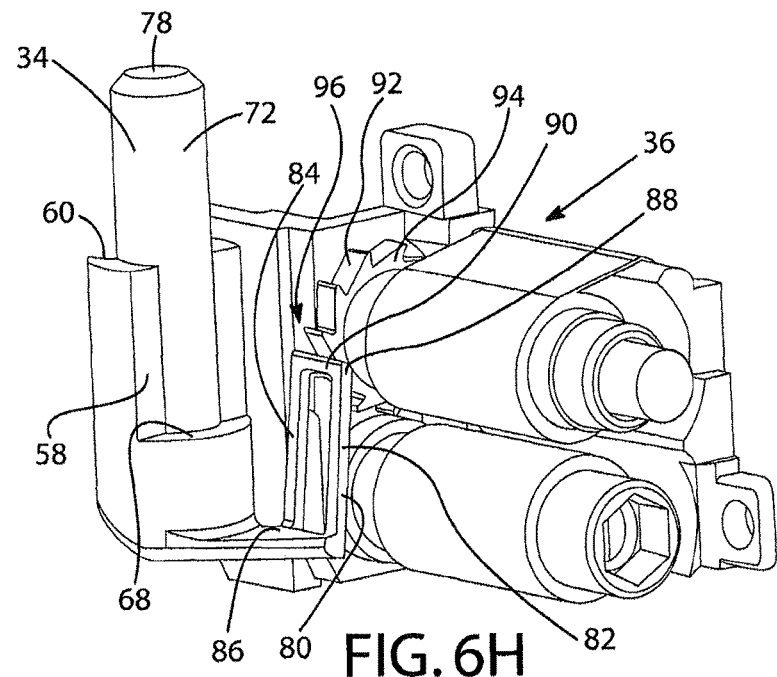


FIG. 6H

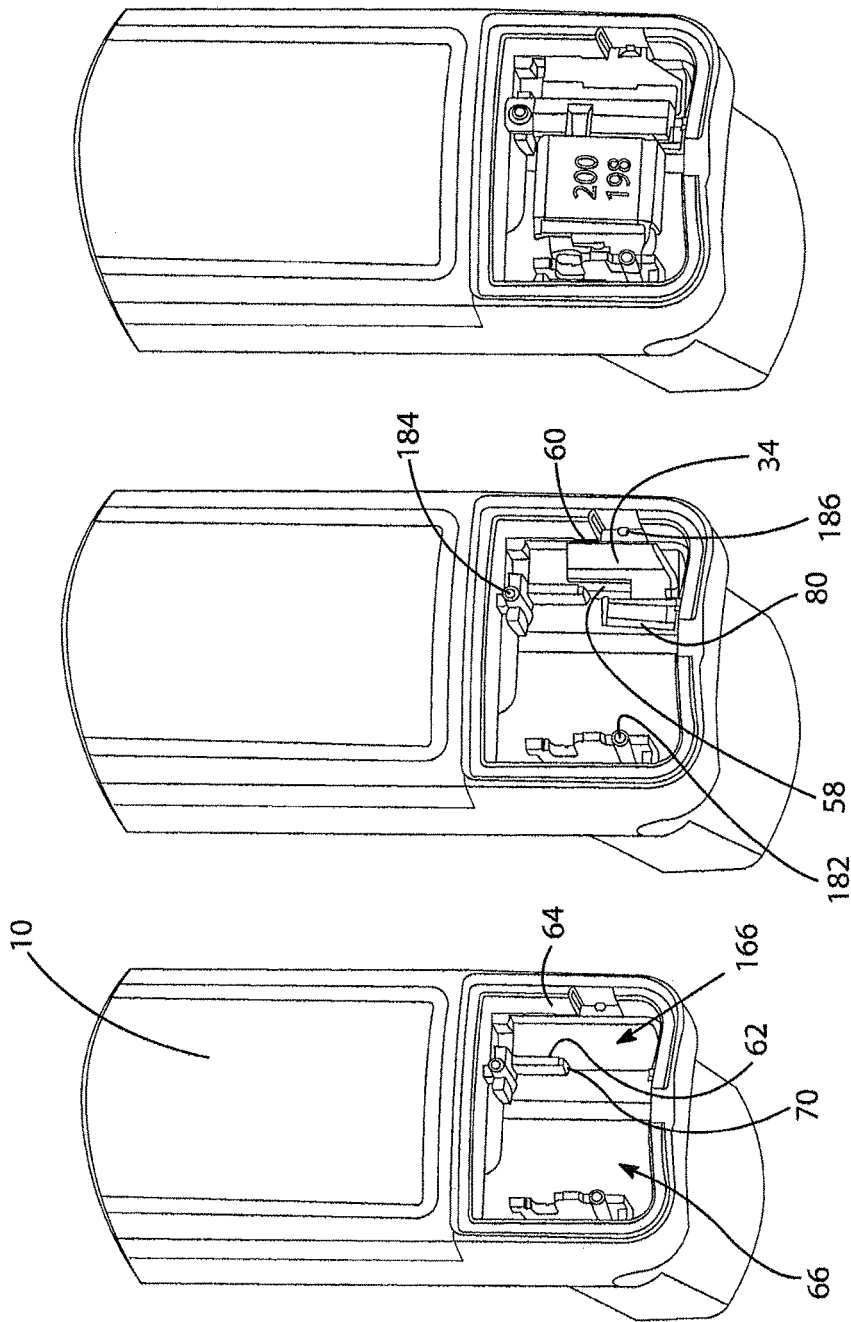


FIG. 8C

FIG. 8B

FIG. 8A

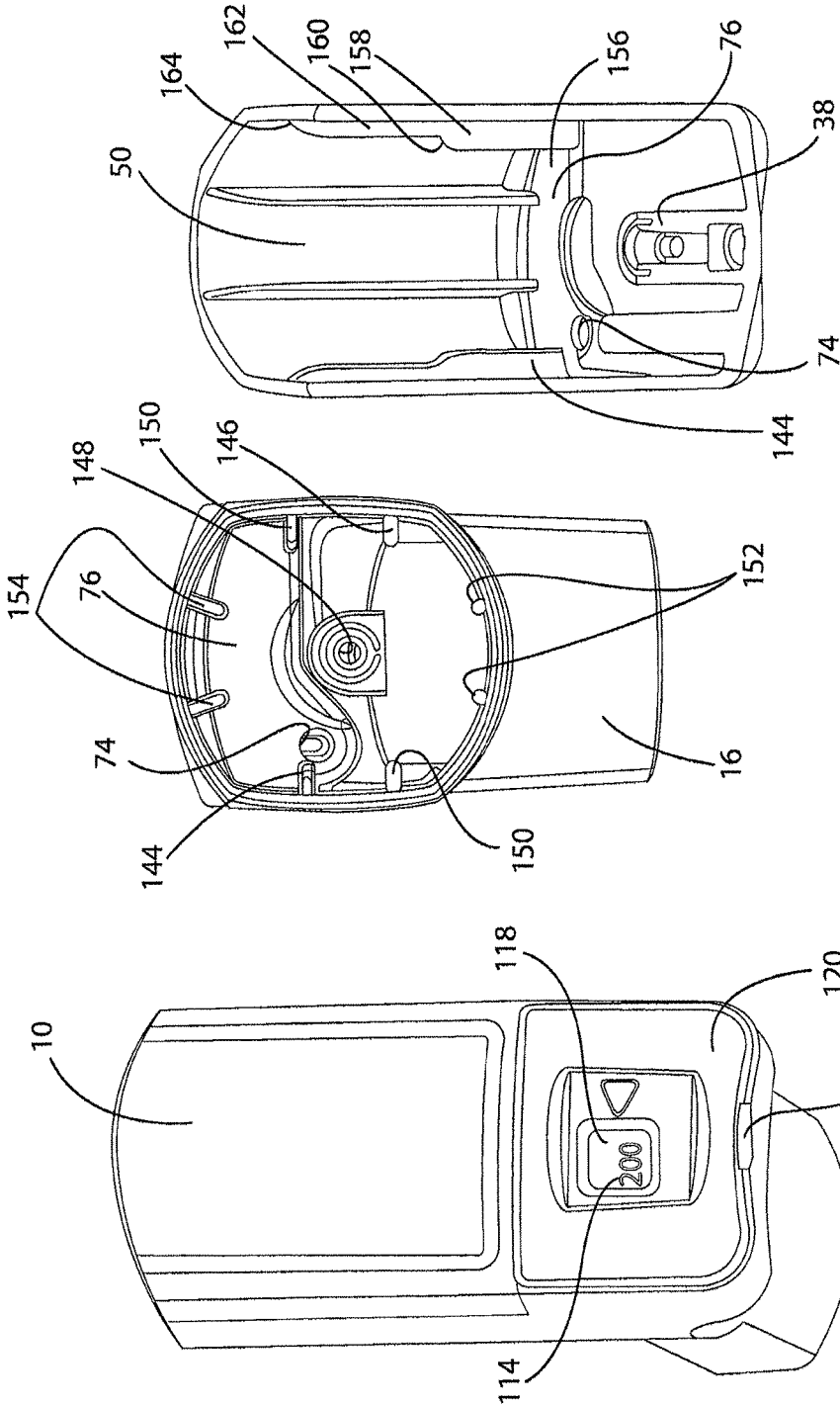
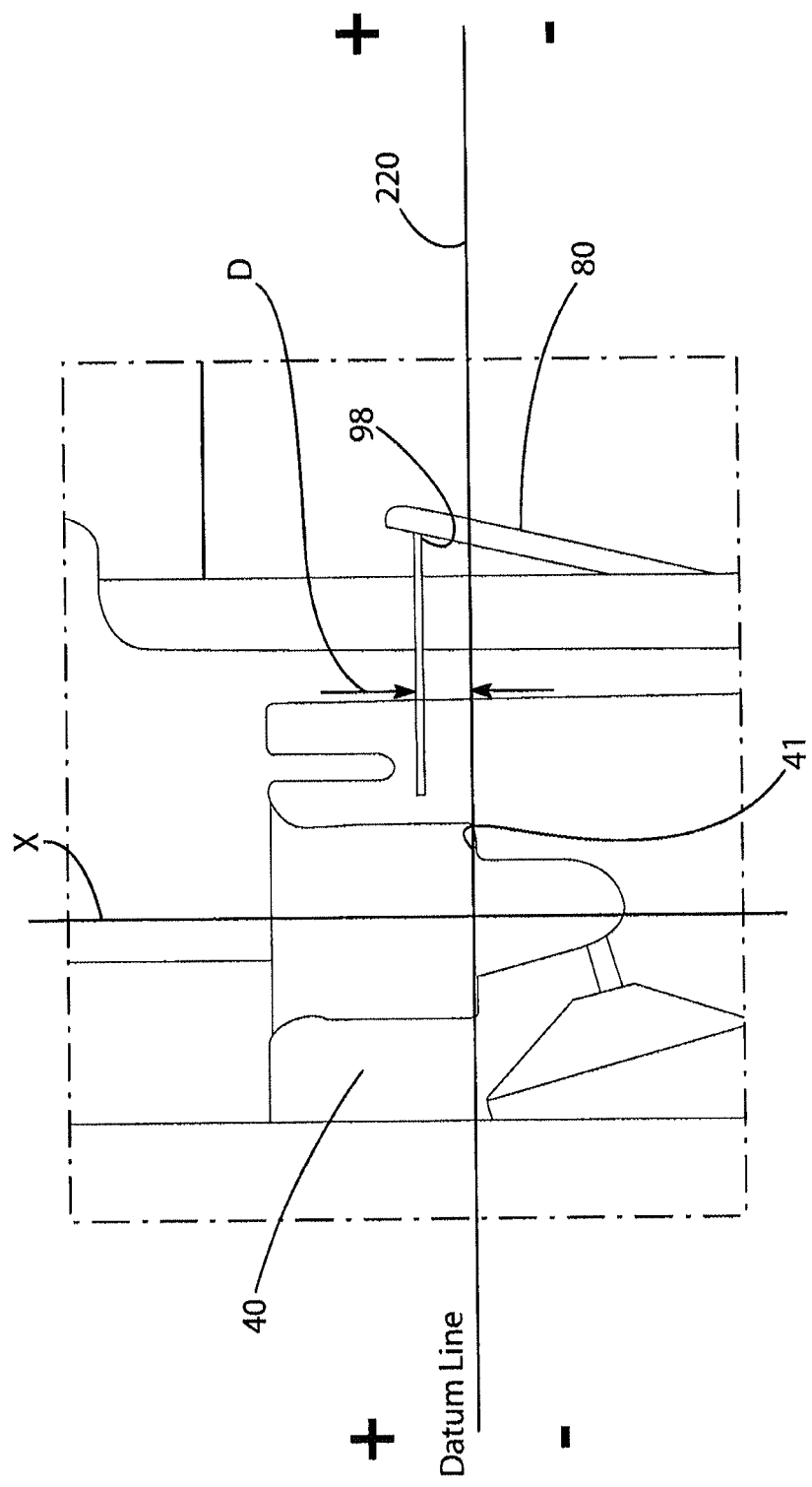


FIG. 7C

FIG. 7D

FIG. 8D



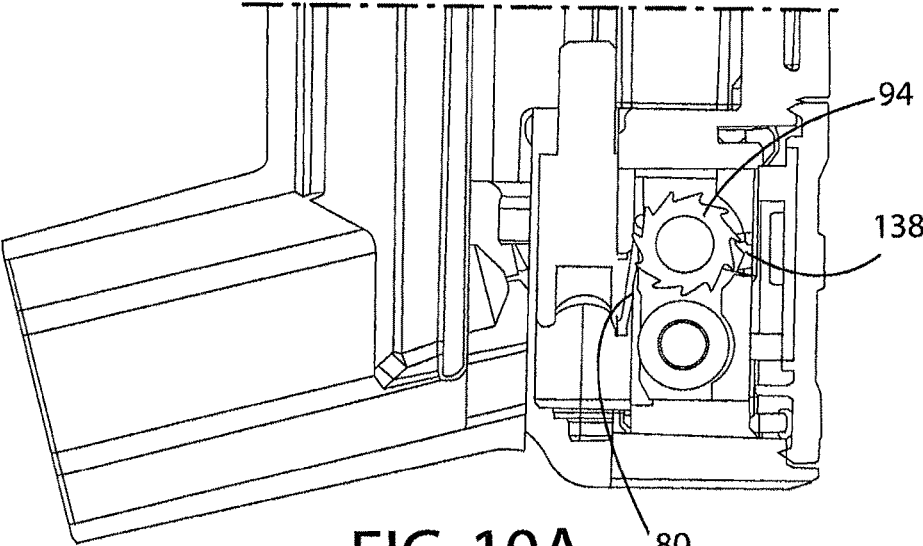


FIG. 10A

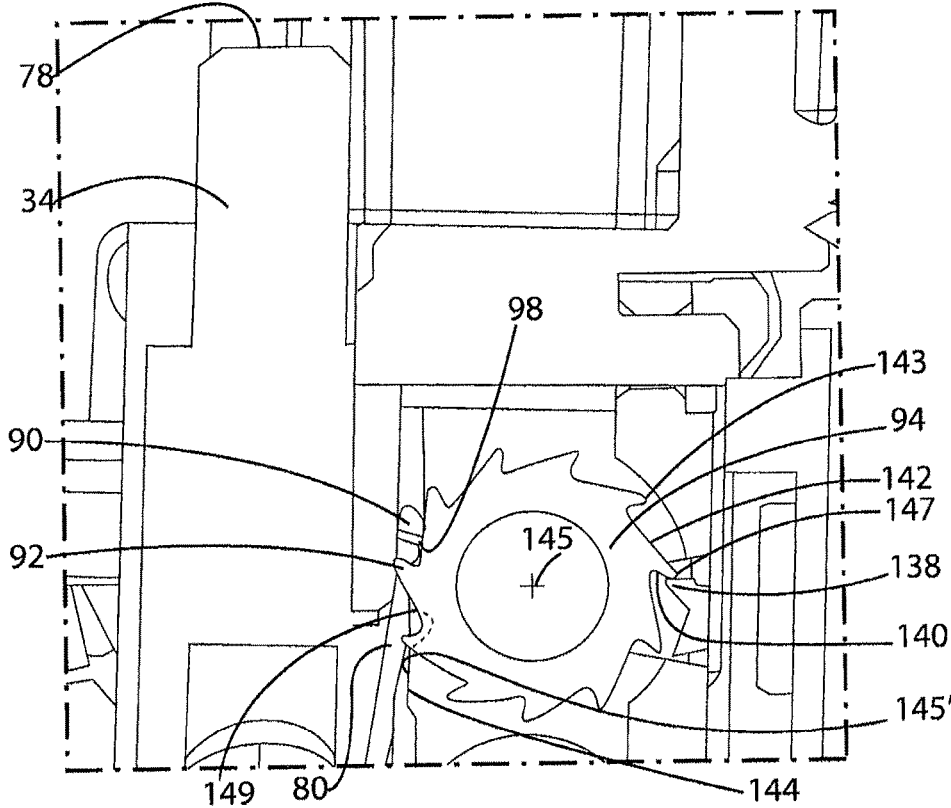


FIG. 10B

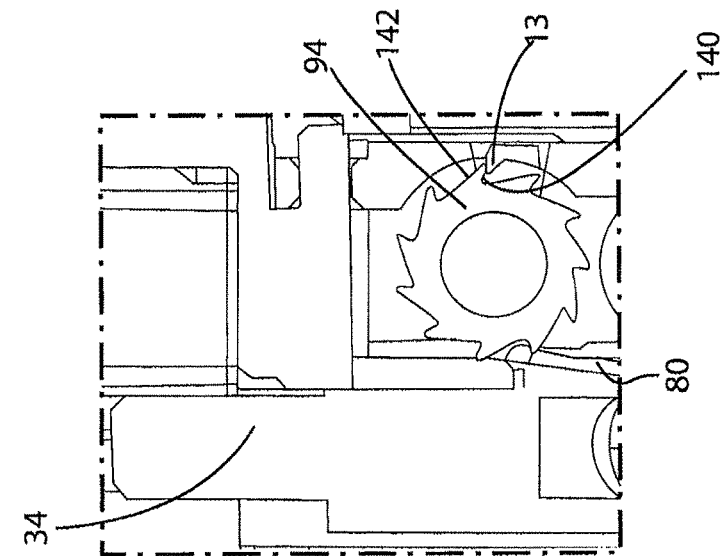


FIG. 10E

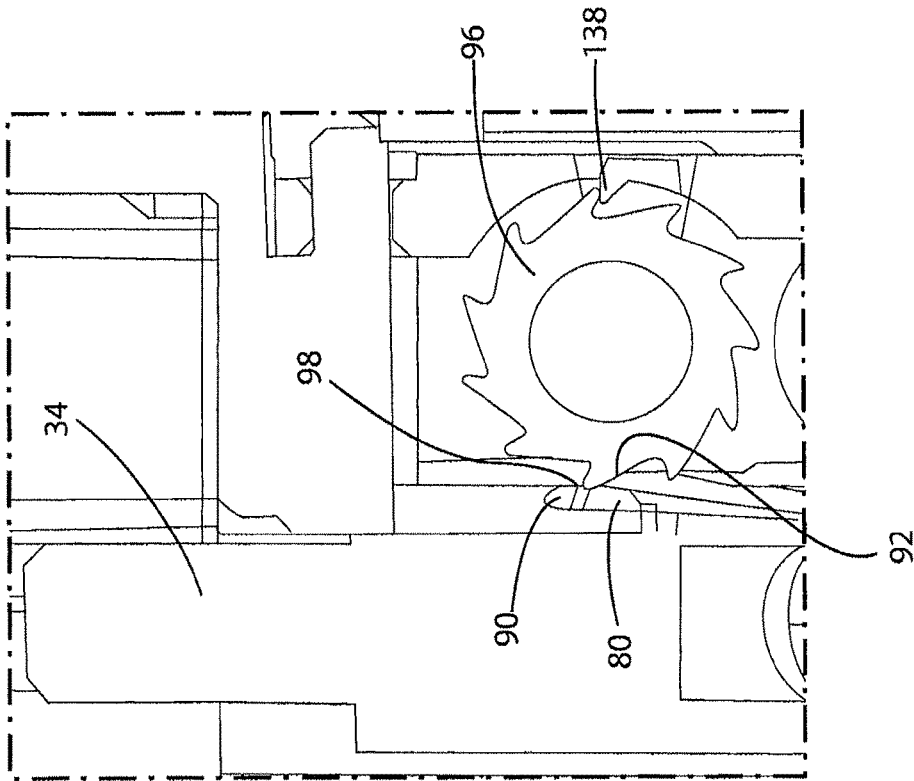


FIG. 10C

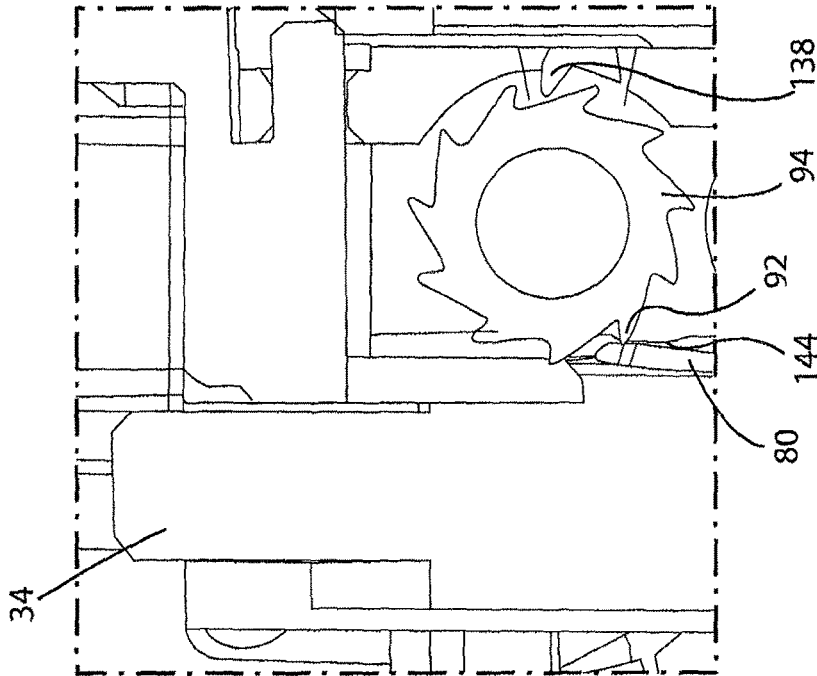


FIG. 10F

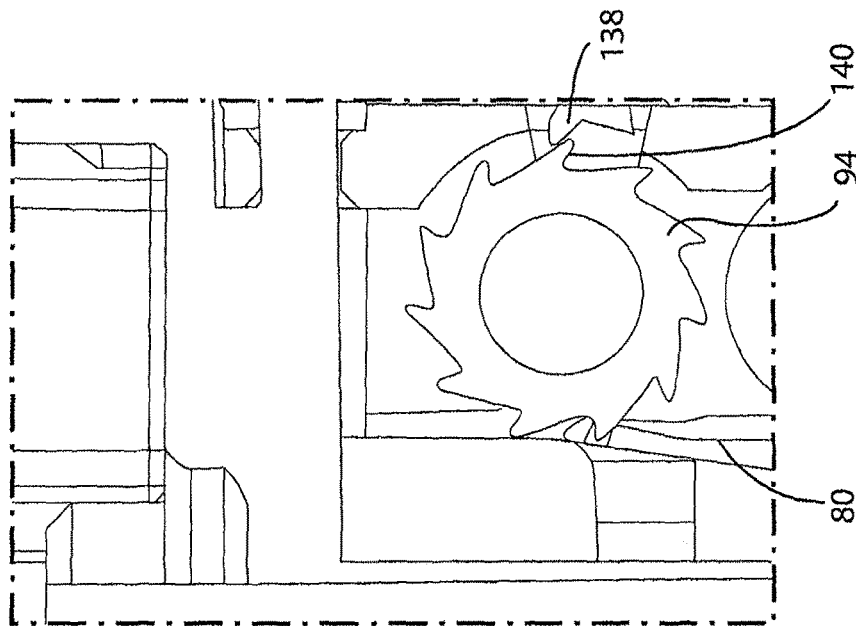


FIG. 10D

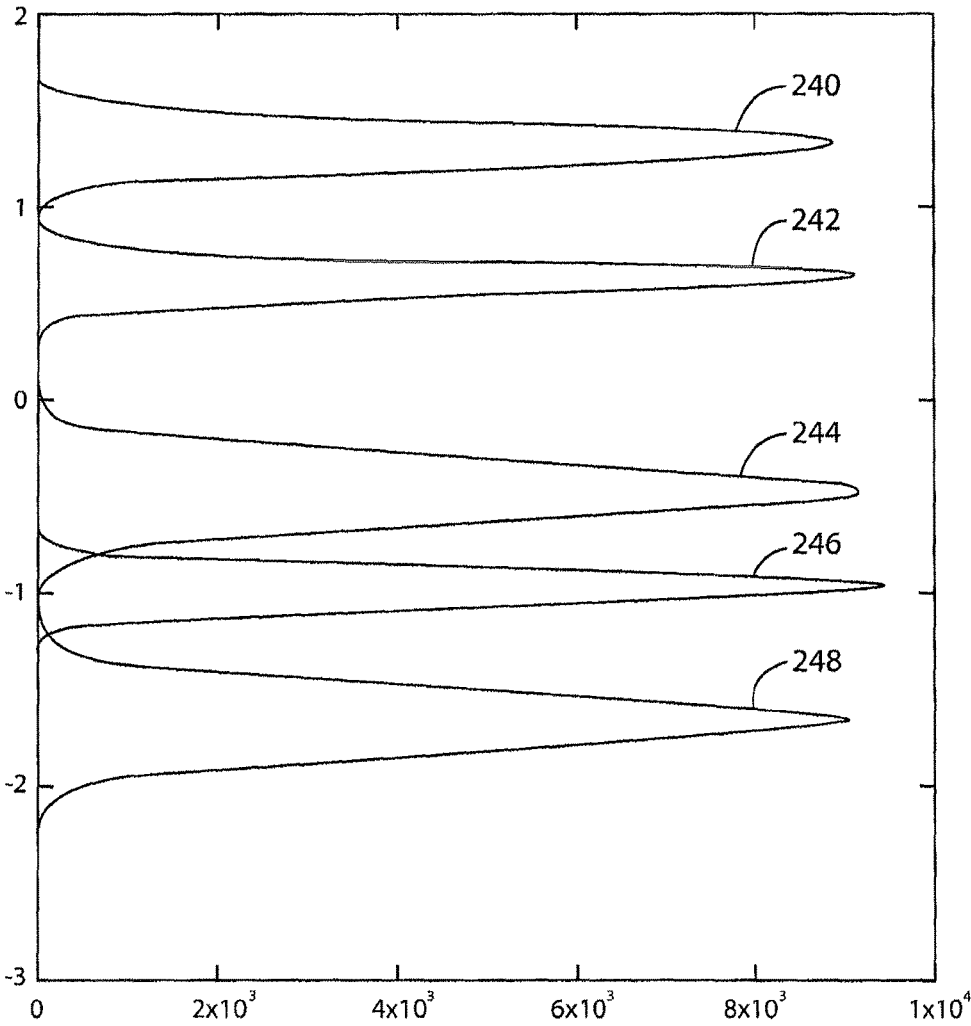


FIG. 11

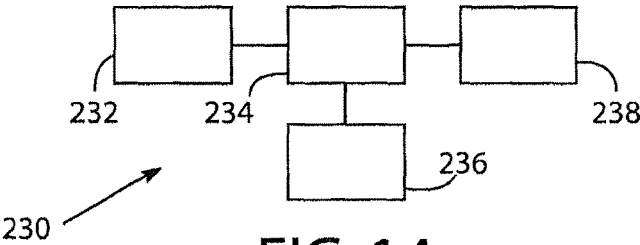


FIG. 14

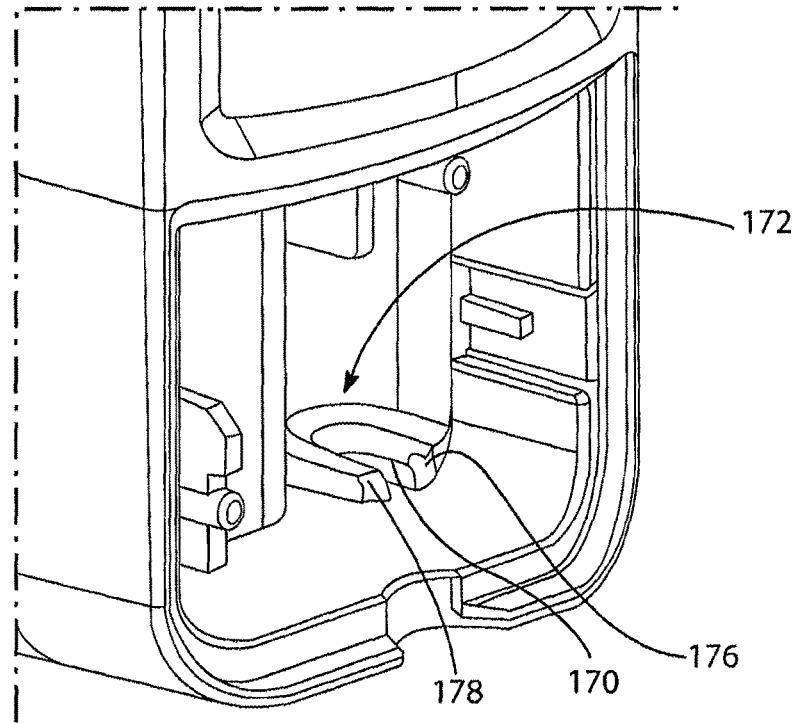


FIG. 12

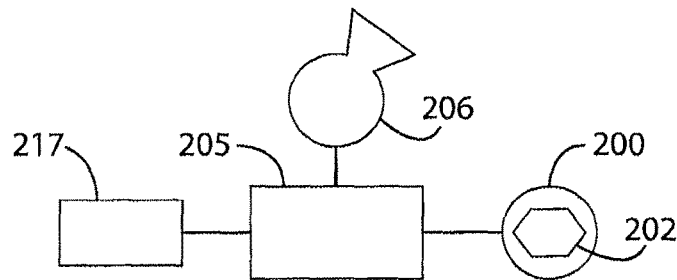
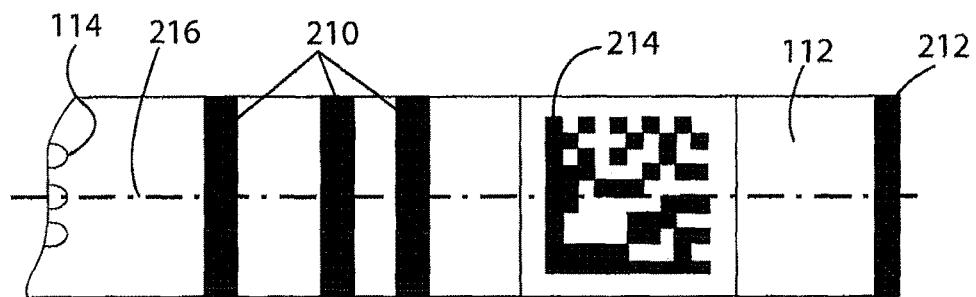


FIG. 13

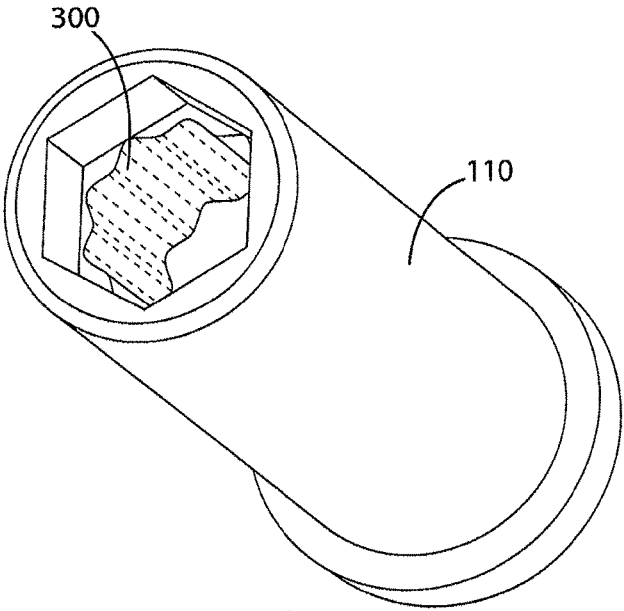


FIG. 15

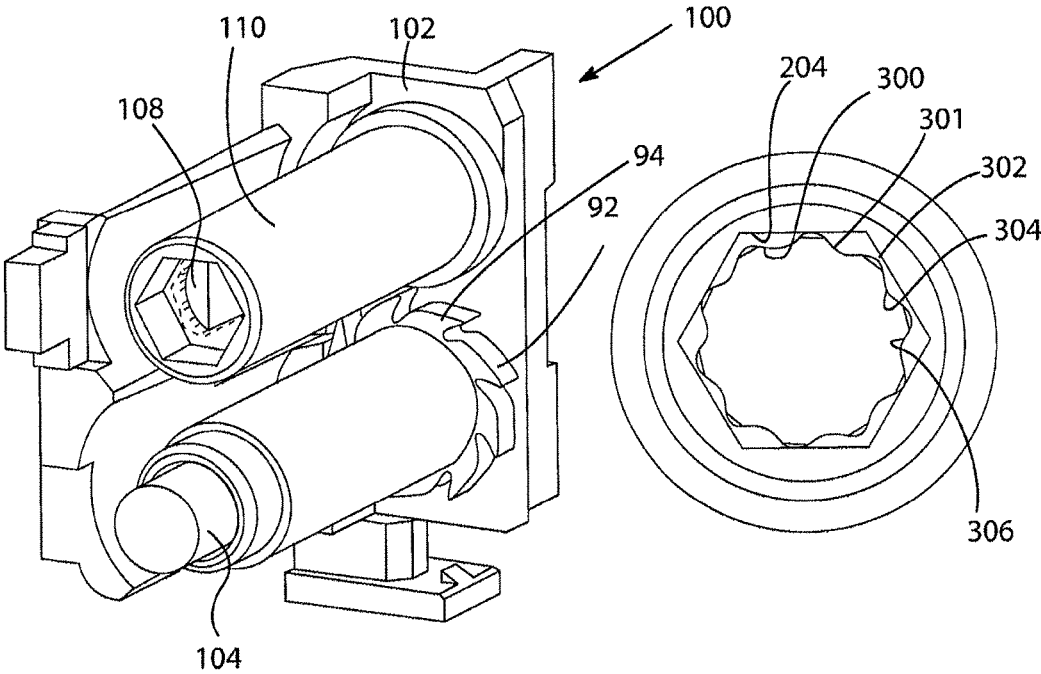


FIG. 20

FIG. 16

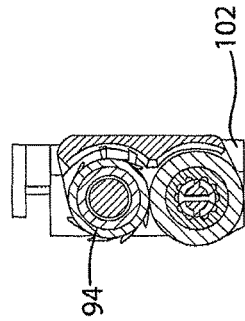


FIG. 18A

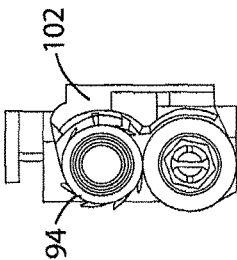


FIG. 18B

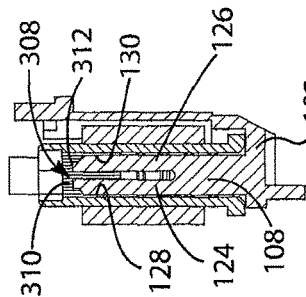


FIG. 18C

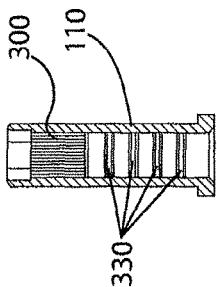


FIG. 17

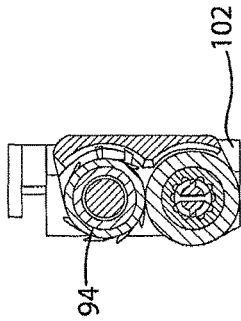


FIG. 19A

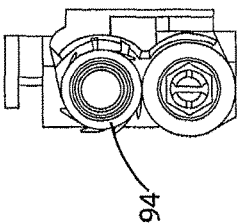


FIG. 19B

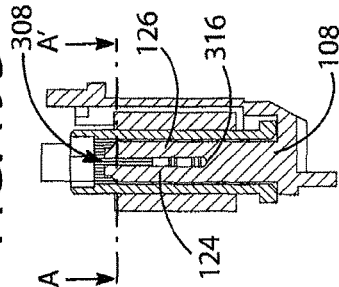


FIG. 19C

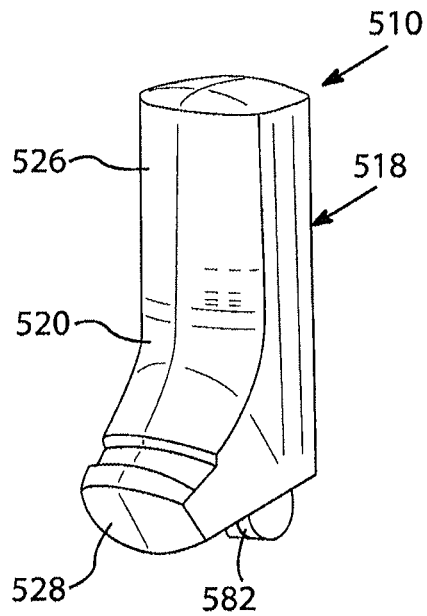


FIG. 21

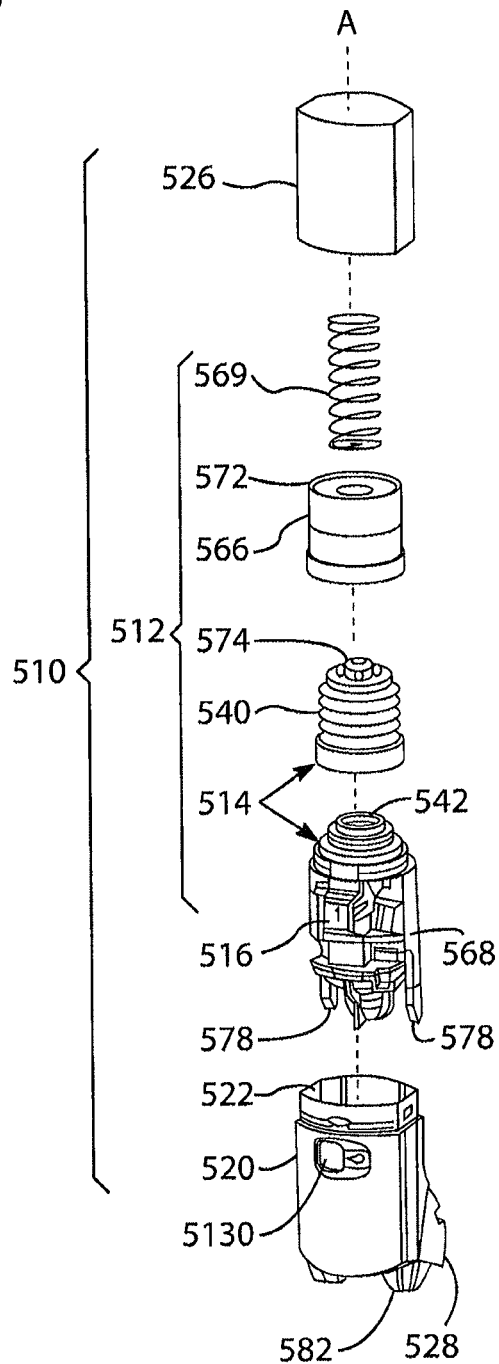


FIG. 22

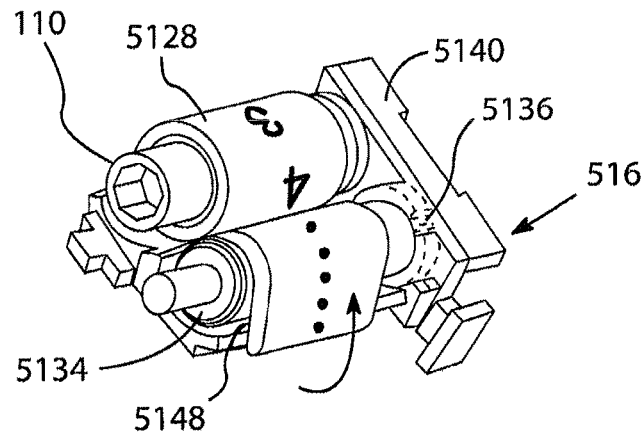


FIG. 23

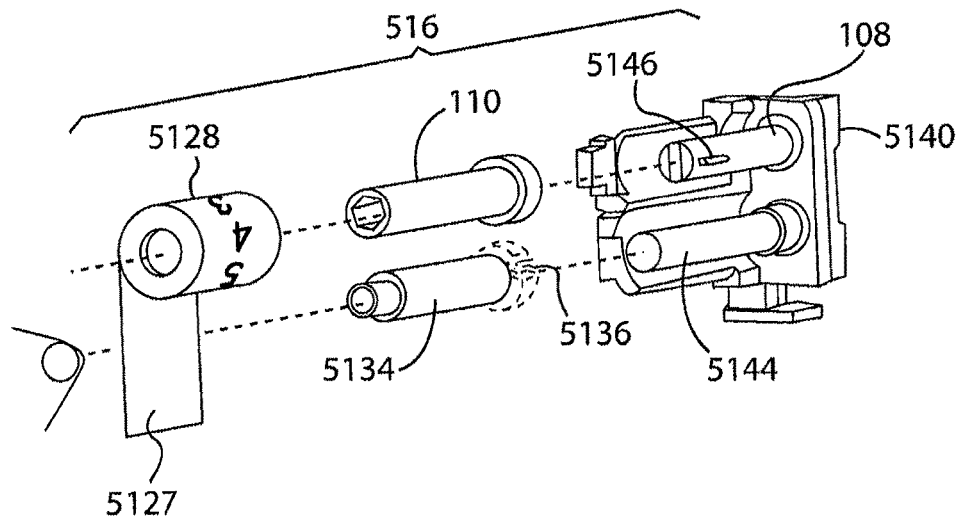


FIG. 24

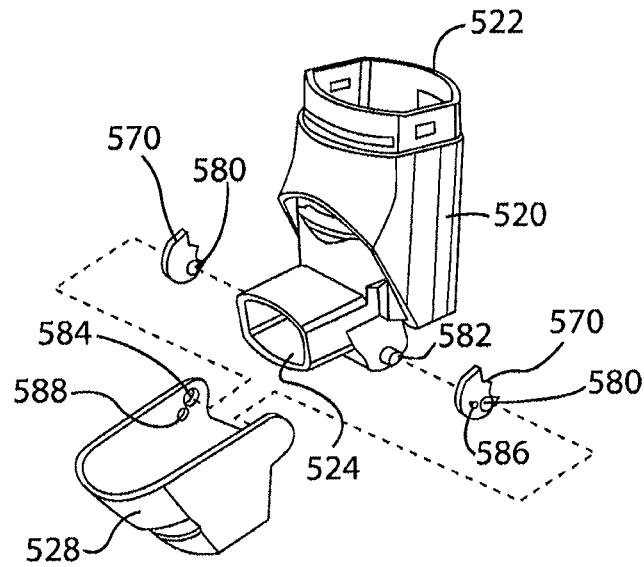


FIG. 25

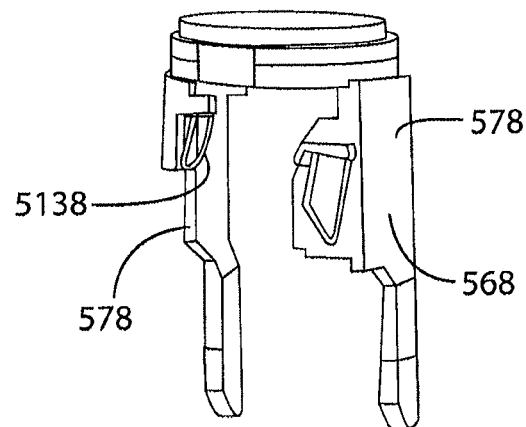


FIG. 26

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**DOSE COUNTER FOR INHALER HAVING A
BORE AND SHAFT ARRANGEMENT****CROSS-REFERENCE TO RELATED
APPLICATIONS**

This patent application is a continuation patent application of U.S. Non-Provisional patent application Ser. No. 14/699,578, filed Apr. 29, 2015, which is a continuation patent application of U.S. Non-Provisional patent application Ser. No. 14/103,353, filed Dec. 11, 2013, which is a divisional patent application of U.S. Non-Provisional patent application Ser. No. 13/110,532, filed May 18, 2011, now U.S. Pat. No. 8,978,966, issued Mar. 17, 2015, which claims priority to U.S. Provisional Patent Application No. 61/345,763, filed May 18, 2010, and U.S. Provisional Patent Application No. 61/417,659, filed Nov. 29, 2010, each of which is incorporated herein by reference in its entirety for all purposes.

FIELD OF THE INVENTION

The present invention relates to dose counters for inhalers, inhalers and methods of assembly thereof. The invention is particularly applicable to metered dose inhalers including dry power medicament inhalers, breath actuated inhalers and manually operated metered dose medicament inhalers.

BACKGROUND OF THE INVENTION

Metered dose inhalers can comprise a medicament-containing pressurised canister containing a mixture of active drug and propellant. Such canisters are usually formed from a deep-drawn aluminium cup having a crimped lid which carries a metering valve assembly. The metering valve assembly is provided with a protruding valve stem which, in use is inserted as a push fit into a stem block in an actuator body of an inhaler having a drug delivery outlet. In order to actuate a manually operable inhaler, the user applies by hand a compressive force to a closed end of the canister and the internal components of the metering valve assembly are spring loaded so that a compressive force of approximately 15 to 30 N is required to activate the device in some typical circumstances.

In response to this compressive force the canister moves axially with respect to the valve stem and the axial movement is sufficient to actuate the metering valve and cause a metered quantity of the drug and the propellant to be expelled through the valve stem. This is then released into a mouthpiece of the inhaler via a nozzle in the stem block, such that a user inhaling through the outlet of the inhaler will receive a dose of the drug.

A drawback of self-administration from an inhaler is that it is difficult to determine how much active drug and/or propellant are left in the inhaler, if any, especially of the active drug and this is potentially hazardous for the user since dosing becomes unreliable and backup devices not always available.

Inhalers incorporating dose counters have therefore become known.

WO 98/028033 discloses an inhaler having a ratchet mechanism for driving a tape drive dose counter. A shaft onto which tape is wound has a friction clutch or spring for restraining the shaft against reverse rotation.

EP-A-1486227 discloses an inhaler for dry powered medicament having a ratchet mechanism for a tape dose counter which is operated when a mouthpiece of the inhaler

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is closed. Due to the way in which the mouthpiece is opened and closed, and actuation pawl of the device which is mounted on a yoke, travels a known long stroke of consistent length as the mouthpiece is opened and closed.

5 WO 2008/119552 discloses a metered-dose inhaler which is suitable for breath-operated applications and operates with a known and constant canister stroke length of 3.04 mm+/-0.255 mm. A stock bobbin of the counter, from which a tape is unwound, rotates on a shaft having a split pin intended to hold the stock bobbin taut. However, some dose counters do not keep a particularly reliable count, such as if they are dropped onto a hard surface.

10 More recently, it has become desirable to improve dose counters further and, in particular, it is felt that it would be useful to provide extremely accurate dose counters for manually-operated canister-type metered dose inhalers. Unfortunately, in these inhalers, it has been found in the course of making the present invention that the stroke length of the canister is to a very large extent controlled on each dose operation by the user, and by hand. Therefore, the stroke length is highly variable and it is found to be extremely difficult to provide a highly reliable dose counter for these applications. The dose counter must not count a dose when the canister has not fired since this might wrongly indicate to the user that a dose has been applied and if done repeatedly the user would throw away the canister or whole device before it is really time to change the device due to the active drug and propellant reaching a set minimum. Additionally, the canister must not fire without the dose counter counting because the user may then apply another dose thinking that the canister has not fired, and if this is done repeatedly the active drug and/or propellant may run out while the user thinks the device is still suitable for use according to the counter. It has also been found to be fairly difficult to assembly some known inhaler devices and the dose counters therefor. Additionally, it is felt desirable to improve upon inhalers by making them easily usable after they have been washed with water.

20 25 30 35 40 The present invention aims to alleviate at least to a certain extent one or more of the problems of the prior art.

SUMMARY OF THE INVENTION

According to a first aspect of the present invention there is provided a dose counter for an inhaler, the dose counter having a counter display arranged to indicate dosage information, a drive system arranged to move the counter display incrementally in a first direction from a first station to a second station in response to actuation input, wherein a regulator is provided which is arranged to act upon the counter display at the first station to regulate motion of the counter display at the first station to incremental movements.

The regulator is advantageous in that it helps prevent unwanted motion of the counter display if the counter is dropped.

According to a further aspect of the present invention, the regulator provides a resistance force of greater than 0.1 N against movement of the counter display. According to still a further aspect of the present invention, the resistance force is greater than 0.3 N. According to yet a further aspect of the present invention, the resistance force is from 0.3 to 0.4 N.

Preferably, the counter comprises a tape.

60 65 Preferably, the tape has dose counter indicia displayed thereon. The first station may comprise a region of the dose counter where tape is held which is located before a display location, such as a display window, for the counter indicia.

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The first station may comprise a first shaft, the tape being arranged on the first shaft and to unwind therefrom upon movement of the counter display.

The first shaft may be mounted for rotation relative to a substantially rotationally fixed element of the dose counter.

The regulator may comprise at least one projection which is arranged on one of the first shaft and the substantially rotationally fixed element and to engage incrementally with one or more formations on the other of the first shaft and the substantially rotationally fixed element.

At least two said projections may be provided. Exactly two said projections may be provided.

Each projection may comprise a radiused surface.

The at least one projection may be located on the substantially fixed element which may comprise a fixed shaft which is fixed to a main body of the dose counter, the first shaft being rotationally mounted to the fixed shaft.

Preferably, the fixed shaft has at least two resiliently flexible legs (or forks). Each leg may have at least one said projection formed in an outwardly facing direction thereon, said one or more formations being formed on an inwardly facing engagement surface of the first shaft, said at least one projection being arranged to resiliently engage said one or more formations. Preferably, a series of said formations are provided. An even number of said formations may be provided. Eight to twelve of said formations may be provided. In one embodiment, ten said formations are provided.

Each said formation may comprise a concavity formed on an engagement surface. Each concavity may comprise a radiused surface wall portion which preferably merges on at least one side thereof into a flat wall portion surface. The engagement surface may include a series of said concavities, and convex wall portions of the engagement surface may be formed between each adjacent two said concavities, each said convex wall portion comprising a convex radiused wall portion.

Each convex radiused wall portion of each convex wall portion may be connected by said flat wall portion surfaces to each adjacent concavity.

The fixed shaft may comprise a split pin with fork legs and each projection may be located on a said fork leg.

The first shaft may comprise a substantially hollow bobbin.

Said at least one formation may be located on an inner surface of the bobbin. In other embodiments it may be located on an outer surface thereof. Said engagement surface may extend partially along said bobbin, a remainder of the respective inner or outer surface having a generally smooth journal portion along at least a portion thereof.

The drive system may comprise a tooth ratchet wheel arranged to act upon a second shaft which is located at the second station, the second shaft being rotatable to wind the tape onto the second shaft.

The second shaft may be located on a main body of the dose counter spaced from and parallel to the first shaft.

The ratchet wheel may be fixed to the second shaft is arranged to rotate therewith. The ratchet wheel may be secured to an end of the second shaft and aligned coaxially with the second shaft.

The dose counter may include anti-back drive system which is arranged to restrict motion of the second shaft. The anti-back drive system may include a substantially fixed tooth arranged to act upon teeth of the ratchet wheel.

According to a further aspect of the present invention, a dose counter includes an anti-back drive system which is arranged to restrict motion of the second shaft in a tape winding direction.

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According to a further aspect of the present invention there is provided a shaft for holding counter tape in a dose counter for an inhaler, the shaft having an engagement surface including incrementally spaced formations located around a periphery thereof, the formations comprising a series of curved concavities and convex portions.

The shaft may comprise a hollow bobbin.

The engagement surface may be a generally cylindrical inwardly directed surface.

The engagement surface may include a flat surface wall portion joining each concavity and convex wall portion.

Each concavity may comprise a radiused wall portion.

Each convex wall portion may comprise a radiused wall portion.

Said concavities may be regularly spaced around a longitudinal axis of the shaft.

Said convex wall portions may be regularly spaced around a longitudinal axis of the shaft.

In some embodiments there may be from eight to twelve said concavities and/or convex wall portions regularly spaced around a longitudinal axis thereof.

One embodiment includes ten said concavities and/or convex wall portions regularly spaced around a longitudinal axis of the shaft.

According to a further aspect of the present invention there is provided a shaft and counter tape assembly for use in a dose counter for an inhaler, the assembly comprising a rotatable shaft and a counter tape which is wound around the shaft and is adapted to unwind therefrom upon inhaler actuation, the shaft having an engagement surface which includes incrementally spaced formations located around a periphery thereof.

According to a further aspect of the present invention there is provided an inhaler for the inhalation of medication and the like, the inhaler including a dose counter as in the first aspect of the present invention.

A preferred construction consists of a manually operated metered dose inhaler including a dose counter chamber including a dose display tape driven by a ratchet wheel which is driven in turn by an actuator pawl actuated by movement of a canister, the tape unwinding from a stock bobbin during use of the inhaler, a rotation regulator being provided for the stock bobbin and comprising a wavelike engagement surface with concavities which engage against control elements in the form of protrusions on resilient forks of a split pin thereby permitting incremental unwinding of the stock bobbin yet resisting excessive rotation if the inhaler is dropped onto a hard surface.

According to another aspect of the present invention there is provided a dose counter for a metered dose inhaler having a body arranged to retain a medicament canister of predetermined configuration for movement of the canister relative thereto; the dose counter comprising: an incremental counting system for counting doses, the incremental counting system having a main body, an actuator arranged to be driven in response to canister motion and to drive an incremental output member in response to canister motion, the actuator and incremental output member being configured to have predetermined canister fire and count configurations in a canister fire sequence, the canister fire configuration being determined by a position of the actuator relative to a datum at which the canister fires medicament and the count configuration being determined by a position of the actuator relative to the datum at which the incremental count system makes an incremental count, wherein the actuator is

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arranged to reach a position thereof in the count configuration at or after a position thereof in the canister fire configuration.

This arrangement has been found to be highly advantageous since it provides an extremely accurate dose counter which is suitable for use with manually operated metered dose inhalers. It has been found that dose counters with these features have a failure rate of less than 50 failed counts per million full canister activation depressions. It has been found in the course of making the present invention that highly reliable counting can be achieved with the dose counter counting at or soon after the point at which the canister fires. It has been is covered by the present inventors that momentum and motion involved in firing the canister, and in some embodiments a slight reduction in canister back pressure on the user at the time of canister firing, can very reliably result in additional further motion past the count point.

The actuator and incremental counting system may be arranged such that the actuator is displaced less than 1 mm, typically 0.25 to 0.75 mm, more preferably about 0.4 to 0.6 mm, relative to the body between its location in the count and fire configurations, about 0.48 mm being preferred. The canister, which can move substantially in line with the actuator, can reliably move this additional distance so as to achieve very reliable counting.

The incremental count system may comprise a ratchet mechanism and the incremental output member may comprise a ratchet wheel having a plurality of circumferentially spaced teeth arranged to engage the actuator.

The actuator may comprise an actuator pawl arranged to engage on teeth of the ratchet wheel. The actuator pawl may be arranged to be connected to or integral with an actuator pin arranged to engage and be depressed by a medicament canister bottom flange. The actuator pawl may be generally U-shaped having two parallel arms arranged to pull on a central pawl member arranged substantially perpendicular thereto. This provides a very reliable actuator pawl which can reliably pull on the teeth of the ratchet wheel.

The incremental count system may include a tape counter having tape with incremental dose indicia located thereon, the tape being positioned on a tape stock bobbin and being arranged to unwind therefrom.

The actuator and incremental output member may be arranged to provide a start configuration at which the actuator is spaced from the ratchet output member, a reset configuration at which the actuator is brought into engagement with the incremental output member during a canister fire sequence, and an end configuration at which the actuator disengages from the ratchet output during a canister fire sequence.

The actuator may be arranged to be located about 1.5 to 2.0 mm, from its location in the fire configuration, when in the start configuration, about 1.80 mm being preferred.

The actuator may be arranged to be located about 1.0 to 1.2 mm, from its location in the fire configuration, when in the reset configuration, about 1.11 mm being preferred.

The actuator may be arranged to be located about 1.1 to 1.3 mm, from its location in the fire configuration, when in the end configuration, about 1.18 mm being preferred.

These arrangements provide extremely reliable dose counting, especially with manually operated canister type metered dose inhalers.

The main body may include a formation for forcing the actuator to disengage from the incremental output member when the actuator is moved past the end configuration. The formation may comprise a bumped up portion of an other-

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wise generally straight surface against which the actuator engages and along which it is arranged to slide during a canister firing sequence.

The dose counter may include a counter pawl, the counter pawl having a tooth arranged to engage the incremental output member, the tooth and incremental output member being arranged to permit one way only incremental relative motion therebetween. When the incremental output member comprises a ratchet wheel, the tooth can therefore serve as an anti-back drive tooth for the ratchet wheel, thereby permitting only one way motion or rotation thereof.

The counter pawl may be substantially fixedly mounted on the main body of the incremental count system and the counter pawl may be arranged to be capable of repeatedly engaging equi-spaced teeth of the incremental output member in anti-back drive interlock configurations as the counter is operated. The counter pawl may be positioned so that the incremental output member is halfway, or substantially halfway moved from one anti-back drive interlock configuration to the next when the actuator and incremental output member are in the end configuration thereof. This is highly advantageous in that it minimises the risk of double counting or non-counting by the dose counter.

According to a further aspect of the invention there is provided an inhaler comprising a main body arranged to retain a medicament canister of predetermined configuration and a dose counter mounted in the main body.

The inhaler main body may include a canister receiving portion and a separate counter chamber, the dose counter being located within the main body thereof, the incremental output member and actuator thereof inside the counter chamber, the main body of the inhaler having wall surfaces separating the canister-receiving portion and the counter chamber, the wall surfaces being provided with a communication aperture, an actuation member extending through the communication aperture to transmit canister motion to the actuator.

According to a further aspect of the present invention there is a provided an inhaler for metered dose inhalation, the inhaler comprising a main body having a canister housing arranged to retain a medicament canister for motion therein, and a dose counter, the dose counter having an actuation member having at least a portion thereof located in the canister housing for operation by movement of a medicament canister, wherein the canister housing has an inner wall, and a first inner wall canister support formation located directly adjacent the actuation member.

This is highly advantageous in that the first inner wall canister support formation can prevent a canister from rocking too much relative to the main body of the inhaler. Since the canister may operate the actuation member of the dose counter, this substantially improves dose counting and avoids counter errors.

The canister housing may have a longitudinal axis which passes through a central outlet port thereof, the central outlet port being arranged to mate with an outer canister fire stem of a medicament canister, the inner wall canister support formation, the actuation member and the outlet port lying in a common plane coincident with the longitudinal axis. Accordingly, this construction may prevent the canister from rocking towards the position of the dose counter actuation member, thereby minimising errors in counting.

The canister housing may have a further inner canister wall support formation located on the inner wall opposite, or substantially opposite, the actuation member. Accordingly, the canister may be supported against rocking motion away from the actuator member so as to minimise count errors.

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The canister housing may be generally straight and tubular and may have an arrangement in which each said inner wall support formation comprises a rail extending longitudinally along the inner wall.

Each said rail may be stepped, in that it may have a first portion located towards a medicine outlet end or stem block of the canister housing which extends inwardly a first distance from a main surface of the inner wall and a second portion located toward an opposite end of the canister chamber which extends inwardly a second, smaller distance from the main surface of the inner wall. This may therefore enable easy insertion of a canister into the canister housing such that a canister can be lined up gradually in step wise function as it is inserted into the canister housing.

The inhaler may include additional canister support rails which are spaced around an inner periphery of the inner wall of the canister housing and which extend longitudinally therealong.

At least one of the additional rails may extend a constant distance inwardly from the main surface of the inner wall.

At least one of the additional rails may be formed with a similar configuration to the first inner wall canister support formation.

The dose counter may, apart from said at least a portion of the actuation member, be located in a counter chamber separate from the canister housing, the actuation member comprising a pin extending through an aperture in a wall which separates the counter chamber and the canister housing.

According to a further aspect of the present invention there is provided an inhaler for inhaling medicaments having: a body for retaining a medicament store; the body including a dose counter, the dose counter having a moveable actuator and a return spring for the actuator, the return spring having a generally cylindrical and annular end; the body having a support formation therein for supporting said end of the return spring, the support formation comprising a shelf onto which said end is engageable and a recess below the shelf.

This shelf and recess arrangement is highly advantageous since it allows a tool (such as manual or mechanical tweezers) to be used to place the return spring of the actuator onto the shelf with the tool then being withdrawn at least partially via the recess.

The shelf may be U-shaped.

The support formation may include a U-shaped upstanding wall extending around the U-shaped shelf, the shelf and upstanding wall thereby forming a step and riser of a stepped arrangement.

The recess below the shelf may also be U-shaped.

At least one chamfered surface may be provided at an entrance to the shelf. This may assist in inserting the actuator and return spring into position.

A further aspect of the invention provides a method of assembly of an inhaler which includes the step of locating said end of said spring on the shelf with an assembly tool and then withdrawing the assembly tool at least partly via the recess. This assembly method is highly advantageous compared to prior art methods in which spring insertion has been difficult and in which withdrawal of the tool has sometimes accidentally withdrawn the spring again.

The cylindrical and annular end of the spring may be movable in a direction transverse to its cylindrical extent into the shelf while being located thereon.

According to a further aspect of the present invention there is provided an inhaler for inhaling medicament, the inhaler having a body for retaining a medicament store; and

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a dose counter, the dose counter having a moveable actuator and a chassis mounted on the body; the chassis being heat staked in position on the body. This is highly advantageous in that the chassis can be very accurately positioned and held firmly in place, thereby further improving counting accuracy compared to prior art arrangements in which some movement of the chassis relative to the body may be tolerated in snap-fit connections.

The chassis may have at least one of a pin or aperture heat staked to a respective aperture or pin of the body.

The chassis may have a ratchet counter output member mounted thereon.

The ratchet counter output member may comprise a ratchet wheel arranged to reel in incrementally a dose meter tape having a dosage indicia located thereon.

According to a further aspect of the present invention there is provided a method of assembling an inhaler including the step of heat staking the chassis onto the body. The step of heat staking is highly advantageous in fixedly positioning the chassis onto the body in order to achieve highly accurate dose counting in the assembled inhaler.

The method of assembly may include mounting a spring-returned ratchet actuator in the body before heat staking the chassis in place. The method of assembly may include pre-assembling the chassis with a dose meter tape prior to the step of heat staking the chassis in place. The method of assembly may include attaching a dose meter cover onto the body after the heat staking step. The cover may be welded onto the body or may in some embodiments be glued or otherwise attached in place.

According to a further aspect of the present invention there is provided an inhaler for inhaling medicament and having a body, the body have a main part thereof for retaining a medicament store; and a dose counter, the dose counter being located in a dose counter chamber of the body which is separated from the main part of the body, the dose counter chamber of the body having a dosage display and being perforated so as to permit the evaporation of water or aqueous matter in the dose counter chamber into the atmosphere.

This is highly advantageous since it enables the inhaler to be thoroughly washed and the dose counting chamber can thereafter dry out fully.

The display may comprise a mechanical counter display inside the dose counter chamber and a window for viewing the mechanical counter display. The mechanical counter display may comprise a tape. The perforated dose counter chamber may therefore enable reliable washing of the inhaler, if desired by the user, and may therefore dry out without the display window misting up.

The dose counter chamber may be perforated by a drain hole formed through an outer hole of the body. The drain hole may be located at a bottom portion of the body of the inhaler, thereby enabling full draining of the inhaler to be encouraged after washing when the inhaler is brought into an upright position.

According to a further aspect of the present invention there is provided a dose counter for an inhaler, the dose counter having a display tape arranged to be incrementally driven from a tape stock bobbin onto an incremental tape take-up drive shaft, the bobbin having an internal bore supported by and for rotation about a support shaft, at least one of the bore and support shaft having a protrusion which is resiliently biased into frictional engagement with the other of the bore and support shaft with longitudinally extending mutual frictional interaction. This arrangement may provide good friction for the bobbin, thereby improving tape counter

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display accuracy and preventing the bobbin from unwinding undesirably for example if the inhaler is accidentally dropped.

The support shaft may be forked and resilient for resiliently biasing the support shaft and bore into frictional engagement.

The support shaft may have two forks, or more in some cases, each having a radially extending protrusion having a friction edge extending therealong parallel to a longitudinal axis of the support shaft for frictionally engaging the bore of the support shaft with longitudinally extending frictional interaction therebetween.

The bore may be a smooth circularly cylindrical or substantially cylindrical bore.

Each of the above inhalers in accordance with aspects of the present invention may have a medicament canister mounted thereto.

The canister may comprise a pressurised metered dose canister having a reciprocally movable stem extending therefrom and movable into a main canister portion thereof for releasing a metered dose of medicament under pressure, for example by operating a metered dose valve inside the canister body. The canister may be operable by pressing by hand on the main canister body.

In cases in which one or more support rails or inner wall support formations are provided, the canister may at all times when within the canister chamber have a clearance of about 0.25 to 0.35 mm from the first inner wall support formation. The clearance may be almost exactly 0.3 mm. This clearance which may apply to the canister body itself or to the canister once a label has been applied, is enough to allow smooth motion of the canister in the inhaler while at the same time preventing substantial rocking of the canister which could result in inaccurate counting by a dose counter of the inhaler, especially when lower face of the canister is arranged to engage an actuator member of the dose counter for counting purposes.

According to a further aspect of the invention, a method of assembling a dose counter for an inhaler comprises the steps of providing a tape with dosing indicia thereon; providing tape positioning indicia on the tape; and stowing the tape while monitoring for the tape positioning indicia with a sensor. The method advantageously permits efficient and accurate stowing of the tape, e.g. by winding.

The dosing indicia may be provided as numbers, the tape positioning indicia may be provided as one or more lines across the tape. The stowing step comprises winding the tape onto a bobbin or shaft, and, optionally, stopping winding when the positioning indicia are in a predetermined position. The tape may be provided with pixelated indicia at a position spaced along the tape from the positioning indicia. The tape may also be provided with a priming dot.

According to a further aspect of the invention, a tape system for a dose counter for an inhaler has a main elongate tape structure, and dosing indicia and tape positioning indicia located on the tape structure. The tape positioning indicia may comprise at least one line extending across the tape structure. The tape system may comprise pixelated indicia located on the tape structure and spaced from the positioning indicia. The tape system may comprise a priming dot located on the tape structure. The positioning indicia may be located between the timing dot and the pixelated indicia. The main elongate tape structure may have at least one end thereof wound on a bobbin or shaft.

A further aspect of the invention provides a method of designing an incremental dose counter for an inhaler comprising the steps of calculating nominal canister fire and

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dose counter positions for a dose counter actuator of the inhaler; calculating a failure/success rate for dose counters built to tolerance levels for counting each fire of inhalers in which the dose counter actuators may be applied; and selecting a tolerance level to result in said failure/success rate to be at or below/above a predetermined value. This is highly advantageous in that it allows an efficient and accurate prediction of the reliability of a series of inhaler counters made in accordance with the design.

The method of designing may include selecting the failure/success rate as a failure rate of no more than one in 50 million. The method of designing may include setting an average count position for dose counters built to the tolerances to be at or after an average fire position thereof during canister firing motion. The method of designing may include setting the average count position to be about 0.4 to 0.6 mm after the average fire position, such as about 0.48 mm after. The method of designing may include setting tolerances for the standard deviation of the fire position in dose counters built to the tolerances to be about 0.12 to 0.16 mm, such as about 0.141 mm. The method of designing may include setting tolerances for the standard deviation of the count positions in dose counters built to the tolerances to be about 0.07 to 0.09 mm, such as about 0.08 mm. A further aspect of the invention provides a computer implemented method of designing an incremental dose counter for an inhaler which includes the aforementioned method of designing.

A further aspect of the invention provides a method of manufacturing in a production run a series of incremental dose counters for inhalers which comprises manufacturing the series of dose counters in accordance with the aforementioned method of designing.

A further aspect of the invention provides a method of manufacturing a series of incremental dose counters for inhalers, which comprises manufacturing the dose counters with nominal canister fire and dose count positions of a dose counter actuator relative to a dose counter chassis (or inhaler main body), and which includes building the dose counters with the average dose count position in the series being, in canister fire process, at or after the average canister fire position in the series.

According to a further aspect of the invention, the method provides fitting each dose counter in the series of incremental dose counters to a corresponding main body of an inhaler.

These aspects advantageously provide for the production run of a series of inhalers and dose counters which count reliably in operation.

According to a further aspect of the invention, an incremental dose counter for a metered dose inhaler has a body arranged to retain a canister for movement of the canister relative thereto, the incremental dose counter having a main body, an actuator arranged to be driven and to drive an incremental output member in a count direction in response to canister motion, the actuator being configured to restrict motion of the output member in a direction opposite to the count direction. This advantageously enables an inhaler dose counter to keep a reliable count of remaining doses even if dropped or otherwise jolted.

The output member may comprise a ratchet wheel. The actuator may comprise a pawl and in which the ratchet wheel and pawl are arranged to permit only one-way ratcheting motion of the wheel relative to the pawl. The dose counter may include an anti-back drive member fixed to the main body. In a rest position of the dose counter, the ratchet wheel is capable of adopting a configuration in which a back surface of one tooth thereof engages the anti-back drive member and the pawl is spaced from an adjacent back

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surface of another tooth of the ratchet wheel without positive drive/blocking engagement between the pawl and wheel.

BRIEF DESCRIPTION OF THE DRAWINGS

The present invention may be carried out in various ways and preferred embodiment of a dose counter, inhaler and methods of assembly, design and manufacture will now be described with reference to the accompanying drawings in which:

FIG. 1 is an isometric view of a main body of an embodiment of an inhaler related to the invention together with a mouthpiece cap therefor;

FIG. 2 is a top plan view of the components as shown in FIG. 1;

FIG. 3A is a section on the plane 3A-3A in FIG. 2;

FIG. 3B is a view corresponding to FIG. 3A but with a dose counter fitted to the main body of the inhaler;

FIG. 4A is an exploded view of the inhaler main body, mouthpiece cap, dose counter and a dose counter window;

FIG. 4B is a view in the direction 4B in FIG. 4C of a spring retainer of the dose counter;

FIG. 4C is a top view of the spring retainer of FIG. 4B;

FIG. 5 is a bottom view of the assembled inhaler main body, mouthpiece cap, dose counter and dose counter window;

FIGS. 6A, 6B, 6C, 6D, 6E, 6F, 6G and 6H are various views of dose counter components of the inhaler;

FIGS. 7A and 7B are sectional views showing canister clearance inside the main body of the inhaler;

FIG. 7C is a further sectional view similar to that of FIG. 7B but with the canister removed;

FIG. 7D is a top plan view of the inhaler main body;

FIGS. 8A, 8B, 8C and 8D show the inhaler main body and dose counter components during assembly thereof;

FIG. 9 shows a sectional side view of a datum line for an actuator pawl of the dose counter;

FIGS. 10A, 10B, 10C, 10D, 10E and 10F show various side views of positions and configurations of the actuator pawl, a ratchet wheel, and a count pawl;

FIG. 11 shows distributions for tolerances of start, reset, fire, count and end positions for the actuator of the dose counter;

FIG. 12 is an enlarged version of part of FIG. 4A;

FIG. 13 shows an end portion of a tape of the dose counter;

FIG. 14 shows a computer system for designing the dose counter;

FIG. 15 is an isometric view of a stock bobbin modified in accordance with the present invention for use in the dose counter of the inhaler of FIGS. 1 to 14;

FIG. 16 shows an end view of the stock bobbin of FIG. 15;

FIG. 17 is a section through a longitudinal axis of the stock bobbin of FIGS. 15 and 16;

FIGS. 18A, 18B and 18C are views of the stock bobbin of FIGS. 15 to 17 mounted in the dose counter chassis of FIGS. 1 to 14, with the control elements of the forks of the second shaft (or split pin) having a profile slightly different to that in FIG. 6F, with the forks in a compressed configuration;

FIGS. 19A, 19B and 19C are views equivalent to FIGS. 18A to 18C but with the forks in a more expanded configuration due to a different rotational position of the stock bobbin;

FIG. 20 is an isometric view of the chassis assembled and including the stock bobbin of FIGS. 15 to 17 but excluding the tape for reasons of clarity;

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FIG. 21 is a view of a preferred embodiment of a dry powder inhaler in accordance with the present invention;

FIG. 22 is an exploded view of the inhaler of FIG. 21;

FIG. 23 is a view of a dose counter of the inhaler of FIG.

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FIG. 24 is an exploded view of the dose counter shown in FIG. 23;

FIG. 25 is an exploded view of parts of the inhaler of FIG. 21; and

10 FIG. 26 is a view of a yoke of the inhaler of FIG. 21.

DETAILED DESCRIPTION OF THE INVENTION

15 FIG. 1 shows a main body 10 of a manually operated metered dose inhaler 12 in accordance with an embodiment related to the present invention and having a mouthpiece cap 14 securable over a mouthpiece 16 of the main body.

The main body has a canister chamber 18 into which a canister 20 (FIG. 7A) is slideable. The canister 20 has a generally cylindrical main side wall 24, joined by a tapered section 26 to a head portion 28 having a substantially flat lower face 30 which has an outer annular drive surface 32 arranged to engage upon and drive an actuation pin 34 of a dose counter 36 as will be described. Extending centrally and axially from the lower face 30 is a valve stem 38 which is arranged to sealingly engage in a valve stem block 40 of the main body 10 of the inhaler 12. The valve stem block 40 has a passageway 42 leading to a nozzle 44 for directing the contents of the canister 20, namely active drug and propellant, towards an air outlet 46 of the inhaler main body 12. It will be appreciated that due to gaps 48 between the canister 20 and an inner wall 50 of the main body 10 of the inhaler 12 an open top 52 of the main body 10 forms an air inlet into the inhaler 12 communicating via air passageway 54 with the air outlet 46, such that canister contents exiting nozzle 44 mix with air being sucked by the user through the air passageway 54 in order to pass together through the air outlet and into the mouth of the user (not shown).

The dose counter 36 will now be described. The dose counter 36 includes an actuation pin 34 biased upwardly from underneath by a return spring 56 once installed in the main body 10. As best shown in FIGS. 4A, 6H and 8A, the pin 34 has side surfaces 58, 60 arranged to slide between corresponding guide surfaces 62, 64 located in a dose counter chamber 66 of the main body 10, as well as an end stop surface 68 arranged to engage a corresponding end stop 70 formed in the dose counter chamber 66 to limit upward movement of the pin 34. The pin 34 has a top part 72 which is circularly cylindrical and extends through an aperture 74 formed through a separator wall 76 which separates the canister chamber 18 from the dose counter chamber 66. The top part 72 of the pin 34 has a flat top surface 78 which is arranged to engage the outer annular drive surface 32 of the canister 20.

55 The actuation pin 34 is integrally formed with a drive or actuator pawl 80. The actuator pawl 80 has a generally inverted U-shape configuration, having two mutually spaced and parallel arms 82, 84 extending from a base portion of the actuation pin 34, each holding at respective distal ends 88 thereof opposite ends of a pawl tooth member 90 which extends in a direction substantially perpendicular to the arms 82, 84, so as to provide what may be considered a "saddle" drive for pulling on each of the 11 drive teeth 92 of a ratchet wheel 94 of an incremental drive system 96 or ratchet mechanism 96 of the dose counter 36. As shown for example in FIG. 10B, the pawl tooth member 90 has a sharp lower

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longitudinal side edge 98 arranged to engage the drive teeth 92, the edge-to-surface contact provided by this engagement providing very accurate positioning of the actuator pawl 80 and resultant rotational positioning of the ratchet wheel 94.

The dose counter 36 also has a chassis preassembly 100 which, as shown in FIGS. 4A and 6A, includes a chassis 102 having a first shaft 104 receiving the ratchet wheel 94 which is secured to a tape reel shaft 106, and a second shaft (or split pin) 108 which is parallel to and spaced from the first shaft 104 and which slidably and rotationally receives a tape stock bobbin 110.

As shown in FIG. 6B, when the inhaler has not been used at all, the majority of a tape 112 is wound on the tape stock bobbin 110 and the tape 112 has a series of regularly spaced numbers 114 displayed therealong to indicate a number of remaining doses in the canister 20. As the inhaler is repeatedly used, the ratchet wheel 94 is rotated by the actuator pawl 80 due to operation of the actuation pin 34 by the canister 20 and the tape 112 is incrementally and gradually wound on to the tape reel shaft 106 from the second shaft 108. The tape 112 passes around a tape guide 116 of the chassis 102 enabling the numbers 114 to be displayed via a window 118 in a dose counter chamber cover 120 having a dose marker 132 formed or otherwise located thereon.

As shown in FIGS. 6A and 6D, the second shaft 108 is forked with two forks 124, 126. The forks 124, 126 are biased away from one another. The forks have located thereon at diametrically opposed positions on the second shaft 108 friction or control elements 128, 130, one on each fork. Each control element extends longitudinally along its respective fork 124, 126 and has a longitudinally extending friction surface 132, 134 which extends substantially parallel to a longitudinal axis of the second shaft and is adapted to engage inside a substantially cylindrical bore 136 inside the tape stock bobbin 110. This control arrangement provided between the bore 136 and the control elements 128, 130 provides good rotational control for the tape stock bobbin 110 such that it does not unwind undesirably such as when the inhaler is dropped. The tape force required to unwind the tape stock bobbin 110 and overcome this friction force is approximately 0.1 N.

As can be seen in FIG. 6D, as well as FIGS. 6G and 10A to 10F, the chassis 102 is provided with an anti-back drive tooth 138 or count pawl 138 which is resiliently and substantially fixedly mounted thereto. As will be described below and as can be seen in FIGS. 10A to 10F, when the actuation pin 34 is depressed fully so as to fire the metered valve (not shown) inside the canister 20, the actuator pawl 80 pulls down on one of the teeth 92 of the ratchet wheel 94 and rotates the wheel 94 anticlockwise as shown in FIG. 6D so as to jump one tooth 92 past the count pawl 138, thereby winding the tape 112 a distance incrementally relative to the dose marker 122 on the dose counter chamber 120 so as to indicate that one dose has been used.

With reference to FIG. 10B, the teeth of the ratchet wheel 94 have tips 143 which are radiused with a 0.1 mm radius between the flat surfaces 140, 142. The ratchet wheel 94 has a central axis 145 which is 0.11 mm above datum plane 220 (FIG. 9). A top/nose surface 147 of the anti-back drive tooth 138 is located 0.36 mm above the datum plane 220. The distance vertically (i.e. transverse to datum plane 220—FIG. 9) between the top nose surface 147 of the anti-back drive tooth is 0.25 mm from the central axis 145 of the wheel 94. Bump surface 144 has a lateral extent of 0.20 mm, with a vertical length of a flat 145' thereof being 1 mm, the width of the bump surface being 1.22 mm (in the direction of the axis 145), the top 149 of the bump surface 144 being 3.02

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mm vertically below the axis 145, and the flat 145' being spaced a distance sideways (i.e. parallel to the datum plane 220) 2.48 mm from the axis 145. The top surface 78 of the pin 34 (FIG. 6H) is 11.20 mm above the datum plane 220 (FIG. 9) when the actuator pawl 80 and pin 34 are in the start configuration. The length of the valve stem 22 is 11.39 mm and the drive surface 32 of the canister 20 is 11.39 mm above the datum plane 220 when the canister is at rest waiting to be actuated, such that there is a clearance of 0.19 mm between the canister 20 and the pin 34 in this configuration.

FIGS. 10A and 10B show the actuator pawl 80 and ratchet wheel 94 and count pawl 138 in a start position in which the flat top 78 of the pin 34 has not yet been engaged by the outer annular drive surface 32 of the canister 20 or at least has not been pushed down during a canister depression.

In this “start” position, the count pawl 138 engages on a non-return back surface 140 of one of the teeth 92 of the ratchet wheel 94. The lower side edge 98 of the actuator pawl is a distance “D” (FIG. 9) 1.33 mm above datum plane 220 which passes through bottom surface or shoulder 41 of valve stem block 40, the datum plane 220 being perpendicular to a main axis “X” of the main body 10 of the inhaler 12 which is coaxial with the centre of the valve stem block bore 43 and parallel to a direction of sliding of the canister 20 in the main body 10 of the inhaler 12 when the canister is fired.

As shown in FIG. 10B, an advantageous feature of the construction is that the pawl tooth/actuator 90 acts as a supplementary anti-back drive member when the inhaler 12 is not being used for inhalation. In particular, if the inhaler 12 is accidentally dropped, resulting in a jolt to the dose counter 36 then, if the wheel 94 would try to rotate clockwise (backwards) as shown in FIG. 10B, the back surface 140 of a tooth will engage and be blocked by the tooth member 90 of the pawl 80. Therefore, even if the anti-back drive tooth 138 is temporarily bent or overcome by such a jolt, undesirable backwards rotation of the wheel 94 is prevented and, upon the next canister firing sequence, the pawl 90 will force the wheel 94 to catch up to its correct position so that the dose counter 36 continues to provide correct dosage indication.

FIG. 10C shows a configuration in which the actuator pawl 80 has been depressed with the pin 34 by the canister 20 to a position in which the side edge 98 of the pawl tooth member 90 is just engaged with one of the teeth 92 and will therefore upon any further depression of the pin 34 begin to rotate the wheel 94. This is referred to as a “Reset” position or configuration. In this configuration, the lower side edge 98 of the actuator 80 is 0.64 mm above the datum plane 220.

FIG. 10D shows a configuration in which the actuator pawl 80 has been moved to a position lower than that shown in FIG. 10C and in which the metered dose valve (not shown) inside the canister has at this very position fired in order to eject active drug and propellant through the nozzle 44. It will be noted that in this configuration the count pawl 138 is very slightly spaced from the back surface 140 of the same tooth 92 that it was engaging in the configuration of FIG. 10D. The configuration shown in FIG. 10D is known as a “Fire” configuration. In this configuration the lower side edge 98 of the actuator 80 is 0.47 mm below the datum plane 220.

FIG. 10E shows a further step in the sequence, called a “Count” position in which the actuator pawl 80 has rotated the ratchet wheel 94 by the distance circumferentially angularly between two of the teeth 92, such that the count pawl 138 has just finished riding along a forward surface 142 of one of the teeth 92 and has resiliently jumped over the tooth

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into engagement with the back surface **140** of the next tooth. Accordingly, in this "Count" configuration, a sufficiently long stroke movement of the pin **34** has occurred that the tape **112** of the dose counter **36** will just have counted down one dose. In this configuration, the lower side edge **98** of the actuator is 0.95 mm below the datum plane **220**. Accordingly, in this position, the actuator **80** generally, including edge **98**, is 0.48 mm lower than in the fire configuration. It has been found that, although the count configuration happens further on than the fire configuration, counting is highly reliable, with less than 50 failed counts per million. This is at least partially due to momentum effects and to the canister releasing some back pressure on the user in some embodiments as its internal metering valve fires.

In the configuration of FIG. **10F**, the pawl **80** has been further depressed with the pin **34** by the canister **20** to a position in which it is just disengaging from one of the teeth **92** and the actuator pawl **80** is assisted in this disengagement by engagement of one of the arms **84** with a bump surface **144** on the chassis **102** (see FIG. **6G**) and it will be seen at this point of disengagement, which is called an "End" configuration, the count pawl **138** is positioned exactly halfway or substantially halfway between two of the drive teeth **92**. This advantageously means therefore that there is a minimum chance of any double counting or non-counting, which would be undesirable. In the end configuration, the side edge **98** of the actuator is 1.65 mm below the datum plane **220**. It will be appreciated that any further depression of the actuator pawl **80** and pin **34** past the "End" configuration shown in FIG. **10F** will have no effect on the position of the tape **112** displayed by the dose counter **36** since the actuator pawl **80** is disengaged from the ratchet wheel **94** when it is below the position shown in FIG. **10F**.

As shown in FIGS. **7C** and **7D**, the inner wall **50** of the main body **10** is provided with a two-step support rail **144** which extends longitudinally along inside the main body and is located directly adjacent the aperture **74**. As shown in FIG. **7B** a diametrically opposed two-step support rail **146** is also provided and this diametrically opposed in the sense that a vertical plane (not shown) can pass substantially directly through the first rail **144**, the aperture **74**, a central aperture **148** of the valve stem block **40** (in which canister stem **25** is located) and the second two-step support rail **146**. As shown in FIG. **7A** and schematically in FIG. **7B**, the rails **144**, **146** provide a maximum clearance between the canister **20** and the rails **144**, **146** in a radial direction of almost exactly 0.3 mm, about 0.25 to 0.35 mm being a typical range. This clearance in this plane means that the canister **20** can only rock backwards and forwards in this plane towards away from the actuation pin **34**. A relatively small distance and this therefore prevents the canister wobbling and changing the height of the actuation pin **34** as to undesirably alter the accuracy of the dose counter **36**. This is therefore highly advantageous.

The inner wall **50** of the main body **10** is provided with two further two-step rails **150** as well as two pairs **152**, **154** of rails extending different constant radial amounts inwardly from the inner wall **50**, so as to generally achieve a maximum clearance of almost exactly 0.3 mm around the canister **20** for all of the rails **144**, **146**, **150**, **152**, **154** spaced around the periphery of the inner wall **50**, in order to prevent undue rocking while still allowing canister motion freely inside the inhaler **12**. It will be clear from FIG. **7C** for example that the two-step rails have a first portion near an outlet end **156** of the canister chamber **18**, the first portion having a substantially constant radial or inwardly-extending width, a first step **160** leading to a second portion **162** of the rail, the

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second portion **102** having a lesser radial or inwardly extending extent than the first portion **156**, and finally a second step **164** at which the rail merges into the main inner wall **50** main surface.

A method of assembling the inhaler **12** will now be described.

With reference to FIG. **8A**, the main body **10** of the inhaler **12** is formed by two or more plastics mouldings which have been joined together to the configuration shown.

As shown in FIG. **8B**, the actuator pawl **80** and pin **34** are translated forward into position into a pin receiving area **166** in the dose counter chamber **66** and the pin **34** and actuator **80** may then be raised until the pin **34** emerges through the aperture **74**.

Next, the return spring **56** may be inserted below the pin **34** and a generally cylindrical annular lower end **168** of the spring **56** may be moved by a tweezer or tweezer-like assembly tool (not shown) into engagement with a shelf **170** of a spring retainer **172** in the dose counter chamber **66**. The spring retainer **172** is U-shaped and the shelf **170** is U-shaped and has a recess **174** formed below it. As shown in FIGS. **4B**, **4C** and **12** shelf **170** includes three chamfer surfaces **176**, **178**, **180** arranged to assist in moving the lower end of the spring **168** into position onto the shelf using the assembly tool (not shown). Once the lower end of the spring **168** is in place, the assembly tool (not shown) can easily be removed at least partly via the recess **174** below the lower end **168** of the spring **56**.

The tape **112** is attached at one end (not shown) to the tape stock bobbin **110** and is wound onto the bobbin by a motor **200** (FIG. **13**) having a hexagonal output shaft **202** which engages in a hexagonal socket **204** (FIG. **6B**) of the bobbin. During winding, the tape is monitored by a sensor **206**, which may be in the form of a camera or laser scanner, which feeds data to a computer controller **205** for the motor **200**. The controller **205** recognises three positioning markers **210** in the form of lines across the tape **112** and stops the motor **202** when the tape **112** is nearly fully wound onto the bobbin **110**, such that the distal end **212** of the tape **112** can be secured, e.g. by adhesive, to the tape reel shaft **106**. The controller **205** also recognises a pixelated tape size marker **214** observed by the sensor **206** and logs in a stocking system data store **217** details of the tape **112** such as the number of numbers **114** on the tape, such as one hundred and twenty or two hundred numbers **114**. Next, the tape reel shaft is wound until an appropriate position of the lines **210** at which a priming dot **216** will, once the bobbin **110** and reel shaft **106** are slid onto the second shaft **108** and second shaft **104**, be in a position to be located in the window **118** when the inhaler **12** is fully assembled. In the embodiments, the bobbin **110** and reel shaft **106** may be slid onto the shafts **108**, **104** before the tape **112** is secured to the reel shaft **106** and the reel shaft may then be wound to position the priming dot **216**.

Next, the assembled dose counter components of the chassis preassembly **100** shown in FIG. **6B** may as shown in FIG. **8C** be inserted into the dose counter chamber **66**, with pins **182**, **184**, **186** formed on the main body **10** in the dose counter chamber **66** passing through apertures or slots **188**, **190**, **192** formed on the chassis **102**, such that the pins **182**, **184**, **186** extend through (or at least into) the apertures or slots **188**, **190**, **192**. With the chassis **102** being relatively firmly pushed towards the main body **10**, the pins **182**, **184**, **186** are then heat staked and the chassis **102** is therefore after this held very firmly in position in the main body and is unable to move, thereby assisting in providing great accuracy for the dose counter **36**. Next, as shown in FIG. **8D**, the

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dose counter chamber cover **120** may be fitted over the dose counter chamber **66** and may be secured in place such as by welding, with the priming dot **216** being displayed through the window.

The user can, when readying the inhaler **12** for first use, prime the inhaler by depressing the canister **20** three times which will bring the first number **114** on the tape into display through the window **118** in place of the priming dot **216**, the number **114** shown in FIG. **8D** being “200”, thereby indicating that 200 doses are remaining to be dispensed from the canister **20** and inhaler **12**.

As shown in FIG. **8D**, and in FIG. **5**, an open drain hole **194** is provided at the bottom of the dose counter chamber **66** by a substantially semi-circular cut-out or recess formation **196** in a lower surface **198** of the main body **10** of the inhaler. Accordingly, if the user (not shown) should decide to wash the main body **10** of the inhaler, for example after encountering an unhygienic situation or simply as a matter of choice, the drain hole **194** allows initial draining of water from inside the dose counter chamber **66** and also thereafter evaporation of water or any aqueous matter in the dose counter chamber **66** so that the window **118** does not mist up undesirably.

FIG. **14** shows a computer system **230** for designing the dose counter **36** and in particular for calculating distributions representative of average positions and standard deviations in a production series of inhalers of the start, reset, fire, count and end positions of the actuator lower side edge **98** relative to the datum plane **220** (FIG. **9**) and therefore of the actuator pawl **80** generally relative to the ratchet wheel **94**, chassis **102** and, when the inhaler **12** is fully assembled, the main body **10** of the inhaler **12**. The computer system **230** includes a data store **232**, a CPU **234**, an input device **236** (such as a keyboard or communication port) and an output device **238** (such as a communications port, display screen and/or printer). A user may enter data via the input device **236** which may be used by the CPU **234** in a mathematical calculation to predict count failure rates when the various dose counters are to be built in a series with dose counter positions set with given averages and standard deviations and taking into account any momentum/inertia effects and metering valve user-back-pressure reduction effect which will occur upon canister firing of a given type of canister. The computer system **230** is thus mathematically used to design the distributions. For the inhaler **12** described herein with the dose counter **36** and canister **20**, the distributions are designed as shown in FIG. **11**. The x axis shows distance of the lower side surface **98** of the actuator **80** above the datum plane **220** and the y axis is representative of the distribution. Thus, curve **240** shows that the start configuration has an average 1.33 mm above the datum plane **200** (standard deviation is 0.1 mm), curve **242** shows that the reset configuration has an average of 0.64 mm above the datum plane **220** (standard deviation is 0.082 mm), curve **244** shows the fire configuration has an average 0.47 mm below the datum plane **220** (standard deviation is 0.141 mm), curve **246** shows the count configuration has an average 0.95 mm below the datum plane **220** (standard deviation is 0.080 mm), and curve **248** shows the end configuration has an average of 1.65 mm below the datum plane **220** (standard deviation is 0.144 mm).

FIGS. **15** to **20** show a version of the inhaler modified in accordance with the present invention. In these drawings, the same reference numerals have been used to those in the earlier drawings to denote the equivalent components. The inhaler **12** is the same as that in FIGS. **1** to **14** apart from the following modifications.

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First, it can be seen that there is a modification in that the drive teeth **92** of the ratchet wheel **94** have a different profile to that in FIGS. **1** to **14**. There are also only nine ratchet teeth **94** in this embodiment instead of eleven.

Additionally, as shown in FIGS. **18C** and **19C**, the control elements **128**, **130** on the forks **124**, **126** of the second shaft **108** have a tapered profile which is different to the profile of the control elements **128**, **130** shown in FIG. **6F**. Either profile can be used in the embodiment of FIGS. **15** to **20** however.

Furthermore, as shown in FIG. **15**, the tape stock bobbin **110** has an inwardly facing generally cylindrical engagement surface **300** with a wavelike form extending partially therealong. The engagement surface **300** has a cross-section **301** perpendicular to the longitudinal length of the stock bobbin **110** which is constant therealong. This cross-section **301** can be seen in FIG. **16** and consists of a series of ten regularly spaced concavities **302** and ten convex wall portions **304**. The convex wall portions **304** are equi-spaced between the concavities **302**. Each concavity **302** has a radius of 0.2 mm. Each convex wall portion **304** also has a radius of 0.2 mm. Finally, the cross section **301** also includes flat wall portions **306** between all of the radiused wall portions of the concavities **302** and convex wall portions **304**. The geometry of the cross-section **301** is therefore defined by the radii of the concavities **302** and convex wall portions **304**, the flat wall portions **306** and the fact that there are ten concavities **302** and convex wall portions **304**.

The minor diameter of the engagement surface **300**, i.e. between the tips of opposite convex wall portions **304**, is 2.46 mm. The major diameter of the engagement surface **300**, i.e. between the outermost portions of the concavities **302**, is 2.70 mm. The undeformed tip to tip maximum diameter of the forks **124**, **126** of the split pin (the second shaft) **108**, i.e. in the region of the maximum radial extent of the control elements **128**, **130**, is 3.1 millimeters and it will therefore be appreciated that the forks **124**, **126** are resiliently compressed once the stock bobbin **110** has been assembled onto the split pin **108** in all rotational configurations of the stock bobbin **110** relative to the split pin **108**. The minimum gap between the forks **124**, **126** in the plane of the cross sections of FIGS. **18C** and **19C** is 1 mm when the split pin **108** is in the undeformed, pre-inserted state. When the split pin **108** is at maximum compression, as shown in FIGS. **18A** to **18C** when the control elements **128**, **130** are shown to be engaged on top of the convex wall portions **304**, the gap **308** between the tips **310**, **312** of the forks **124**, **126** is 0.36 mm. On the other hand, when the split pin **108** is at minimum compression (once inserted into the stock bobbin) as shown in FIGS. **19A** to **19C**, when the control elements **128**, **130** rest in the concavities **302**, the gap between the tips **310**, **312** of the forks **124**, **126** is 0.6 mm. The control elements **128**, **130** are outwardly radiused with a radius also of 0.2 mm such that they can just rest on the concavities **302** with full surface contact (at least at an axial location on the split pin where the tapered control elements are at their maximum radial extent), without rattling in, locking onto or failing to fit in the concavities **302**. The radii of the control elements **128**, **130** is therefore preferably substantially the same as the radii of the concavities **302**.

It will be appreciated that whereas FIGS. **18B** and **19B** are end views along the coaxial axis of the stock bobbin **110** and split pin **108**, FIGS. **18A** and **19A** are cross-sections. FIG. **19A** is a section on the plane A-A' in FIG. **19C** and FIG. **18A** is a section at the same plane, but of course with the stock bobbin **110** rotated relative to the split pin **108**.

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As the inhaler 12 is used and the ratchet wheel 94 rotates in order to count used doses, the stock bobbin rotates incrementally through rotational positions in which rotation is resisted, i.e. due to increasing compression of the split pin 108 at such rotational positions, and rotational positions in which rotation is promoted, i.e. due to decreasing compression of the split pin 108 at such rotational positions and this may involve a click forward of the stock bobbin 110 to the next position equivalent to that in FIGS. 19A to 19C in which the control elements 128, 130 of the split pin art located in the concavities 302. This functionality firstly allows the stock bobbin to unwind during use as required, but also prevents the tape 112 from loosening during transit if the inhaler 12 is dropped, such as onto a hard surface. This is highly advantageous, since the tape 11 is prevented from moving to a position in which it will give an incorrect reading regarding the number of doses in the canister.

During compression and expansion of the forks in the radial direction between the two configurations shown in FIGS. 18C and 19C, the forks 124, 126 rotate about a point 316 on the split pin where the forks 124, 126 come together. This rotational action means that there is a camming action between the forks 124, 126 and the engagement surface 300 without significant friction but, nevertheless, the resilient forces provided by the regulator formed by the engagement surface 300 and forks 124, 126 are able to regulate unwinding of the tape such that it does not easily occur during transit or if the inhaler 12 is dropped. It has been found during testing that a force of 0.3 to 0.4 N needs to be applied to the tape 112 to overcome the regulator at the stock bobbin 110. 0.32 N is achieved with the control elements 128 having the profile shown in FIG. 19C and 0.38 N is achieved with the profile of the control elements 128 altered to be as shown as described with reference to FIG. 6F. These forces are substantially higher than the 0.1 N force mentioned above and undesirable movement of the tape is substantially avoided even if the inhaler is dropped onto a hard surface. The modified arrangement of FIGS. 15 to 20 does not provide this force "constantly" such that there is overall not an undesirably high friction of the tape 112 as it passes over the other components of the dose counter because, due to the incremental nature of the resilient forces at the regulator, the tape 112 can incrementally relax as it slides over the stationary chassis components.

Instead of having ten concavities 302 and convex wall portions 304, other numbers may be used, such as 8 or 12. However, it is preferred to have an even number, especially since two control elements 128, 130 are provided, so that all of the control elements 128, 130 will expand and contract simultaneously. However, other arrangements are envisaged with 3 or more forks and the number of concavities/convex wall portions may be maintained as an integer divisible by the number of forks to maintain a system with simultaneous expansion/contraction. For example, the use of 9, 12 or 15 concavities/convex wall portions with 3 forks is envisaged.

Instead of having the engagement surface 300 on the inside of the stock bobbin 110, it could be placed on the outside of the stock bobbin 110 so as to be engaged by flexible external legs/pawls or similar.

It will be noted that the regulator provided by the engagement surface 300 and forks 124, 126 does not only allow rotation of the stock bobbin in one direction as is the case with the ratchet wheel 94. Rotation in both directions is possible, i.e. forwards and backwards. This means that during assembly, the stock bobbin 110 can be wound backwards during or after fitting the bobbin 100, shaft 106 and tape 112 onto the carriage 102, if desired.

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The stock bobbin 110 and the carriage 102 including the split pin 108 are both moulded of polypropylene material.

It will be seen from FIG. 16 that the cross-sectional shape 301 is not symmetrical within the hexagonal socket 204. This has enabled the hexagonal socket 204 to be maintained at a useful size while still allowing the desired size and geometry of the cross section 301 to fit without interfering with the hexagonal shape of the hexagonal socket 204 and also permits moulding to work during manufacture.

As shown in FIG. 17, the stock bobbin 110 has a series of four circumferential ribs 330 inside it and a spaced therealong. These hold the stock bobbin 110 on the correct side of the mould tool during moulding.

FIGS. 21 and 22 show a preferred embodiment in accordance with the invention of an inhaler 510 for dispensing a dry-powdered medicament in metered doses for patient inhalation. The inhaler 510 is as disclosed in FIGS. 1 to 16 or EP-A-1330280, the contents of which are hereby fully incorporated herein by reference, but with the stock bobbin 110 and second shaft 108 of the dose counter 516 modified so as to be as in FIGS. 15 to 20 hereof. Thus, the dry powder inhaler 510 generally includes a housing 518, and an assembly 512 received in the housing (see FIG. 21). The housing 518 includes a case 520 having an open end 522 and a mouthpiece 524 (FIG. 25) for patient inhalation, a cap 526 secured to and closing the open end 522 of the case 520, and a cover 528 pivotally mounted to the case 520 for covering the mouthpiece 524. As shown in FIG. 22, the inhaler 510 also includes an actuation spring 569, first yoke 566 with opening 572, bellows 540 with crown 574, a reservoir 514, second yoke 568 with hopper 542 and dose counter 516 mounted thereto, and case 520 has transparent window 5130 thereon for viewing dose counter tape indicia 5128. The dose metering system also includes two cams 570 mounted on the mouthpiece cover 528 and movable with the cover 528 between open and closed positions. The cams 570 each include an opening 580 for allowing outwardly extending hinges 582 of the case 520 to pass therethrough and be received in first recesses 584 of the cover 528. The cams 570 also include bosses 586 extending outwardly and received in second recesses 588 of the cover 528, such that the cover 528 pivots about the hinges 582 and the cams 570 move with the cover 528 about the hinges 582. As described in EP-A-1330280, cams 570 act upon cam followers 578 to move second yoke 568 up and down and thereby operate dose counter by engagement of pawl 5138 on the second yoke 568 with teeth 5136. Remaining components of the inhaler are provided as, and operate as described, in EP-A-1330280.

The dose counting system 516 therefore includes a ribbon or tape 5128 (FIGS. 23 & 24), having successive numbers or other suitable indicia printed thereon, in alignment with a transparent window 5130 provided in the housing 18 (see FIG. 22). The dose counting system 516 includes the rotatable stock bobbin 110 (as described above), an indexing spool 5134 rotatable in a single direction, and the ribbon 5128 rolled and received on the bobbin 110 and having a first end 5127 secured to the spool 5134, wherein the ribbon 5128 unrolls from the bobbin 110 so that the indicia are successively displayed as the spool 5134 is rotated or advanced. In FIGS. 23 and 24 the wavelike engagement surface 300 of the bobbin 110 is not shown for the purposes of clarity.

The spool 134 is arranged to rotate upon movement of the yokes 566, 568 to effect delivery of a dose of medicament from reservoir 514, such that the number on the ribbon 5128 is advanced to indicate that another dose has been dispensed by the inhaler 510. The ribbon 5128 can be arranged such

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that the numbers, or other suitable indicia, increase or decrease upon rotation of the spool 5134. For example, the ribbon 5128 can be arranged such that the numbers, or other suitable indicia, decrease upon rotation of the spool 5134 to indicate the number of doses remaining in the inhaler 510. Alternatively, the ribbon 5128 can be arranged such that the numbers, or other suitable indicia, increase upon rotation of the spool 5134 to indicate the number of doses dispensed by the inhaler 10.

The indexing spool 5134 includes radially extending teeth 5136, which are engaged by pawl 5138 extending from a cam follower 578 of the second yoke 568 upon movement of the yoke to rotate, or advance, the indexing spool 5134. More particularly, the pawl 5138 is shaped and arranged such that it engages the teeth 5136 and advances the indexing spool 5134 only upon the mouthpiece cover 528 being closed and the yokes 566, 568 moved back towards the cap 526 of the housing 518.

The dose counting system 516 also includes a chassis 5140 that secures the dose counting system to the hopper 542 and includes shafts 108, 5144 for receiving the bobbin 110 and the indexing spool 5134. As described above with reference to FIGS. 1 to 20, the bobbin shaft 108 is forked and includes radially nubs 5146 for creating a resilient resistance to rotation of the bobbin 110 on the shaft 108 by engaging with the wavelike engagement surface 300 inside the bobbin 110. A clutch spring 5148 is received on the end of the indexing spool 5134 and locked to the chassis 5140 to allow rotation of the spool 5134 in only a single direction.

Various modifications may be made to the embodiment shown without departing from the scope of the invention as defined by the accompanying claims as interpreted under patent law.

What is claimed is:

1. A dose counter for an inhaler, the dose counter having a display tape arranged to be incrementally driven from a tape stock bobbin onto an incremental tape take-up drive shaft, the bobbin having an internal bore supported by and for rotation about a support shaft, at least one of the bore and the support shaft having a radially extending protrusion having a leading portion edge, a trailing portion edge, wherein at least one of the leading portion edge and the trailing portion edge are tapered, and a friction edge between the leading portion edge and the trailing portion edge, wherein the friction edge is substantially parallel to a longitudinal axis of the support shaft and the leading portion edge and trailing portion edge are not parallel to the longitudinal axis of the support shaft, and the friction edge is resiliently biased into frictional engagement with the other of the bore and support shaft with longitudinally extending

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mutual frictional interaction and wherein the friction edge extends further in a longitudinal direction than the protrusion extends radially.

2. The dose counter of claim 1, wherein the support shaft is forked and configured to resiliently bias the support shaft and bore into frictional engagement.

3. The dose counter of claim 2, wherein the support shaft includes a plurality of tines, each of the plurality of tines having the radially extending protrusion.

4. The dose counter of claim 1, wherein at least a portion of the bore is a smooth substantially cylindrical bore.

5. The dose counter of claim 1, wherein the inhaler includes a medicament canister mounted thereto.

6. The dose counter of claim 5, wherein the canister comprises a pressurised metered dose canister having a reciprocally movable stem extending therefrom and movable into a main canister body for releasing a metered dose of medicament under pressure.

7. The dose counter of claim 6, wherein the canister is configured to be manually operable.

8. The dose counter of claim 1, wherein the bore includes a major diameter and a minor diameter, the major diameter being greater than the minor diameter.

9. The dose counter of claim 8, wherein the bore includes a generally cylindrical polygonal shape with a wavelike surface configured to engage the friction edge.

10. The dose counter of claim 1, wherein the bobbin includes an inner wall having a rib configured to extend from the inner wall into the internal bore.

11. The dose counter of claim 10, wherein the rib is one of a plurality of ribs, each of the plurality of ribs being spaced from another of the plurality of ribs.

12. The dose counter of claim 1, wherein each of the leading portion edge and the trailing portion edge are tapered.

13. The dose counter of claim 1, wherein the leading portion edge is disposed at a first angle relative to the longitudinal axis of the support shaft,

wherein the trailing portion edge is disposed at a second angle relative to the longitudinal axis of the support shaft, and

wherein the first angle is different than the second angle.

14. The dose counter of claim 1, wherein the friction edge is longer along the longitudinal axis than the leading portion edge.

15. The dose counter of claim 1, wherein the friction edge is longer along the longitudinal axis than the trailing portion edge.

16. The dose counter of claim 1, wherein the friction edge is longer along the longitudinal axis than the each of the leading portion edge and the trailing portion edge.

* * * * *

EXHIBIT D

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(45) **Date of Patent:** **Jul. 17, 2018**

(54) **DOSE COUNTERS FOR INHALERS, INHALERS AND METHODS OF ASSEMBLY THEREOF**

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(58) **Field of Classification Search**
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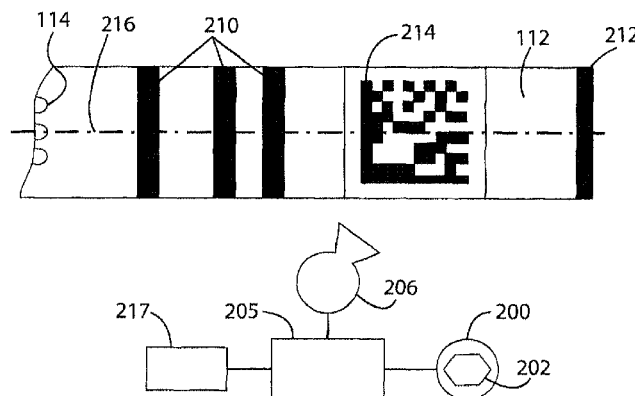
(57) **ABSTRACT**

A tape system for a dose counter for an inhaler, the tape system having a main elongate tape structure, dosing indicia located on the main elongate tape structure, tape positioning indicia located on the main elongate tape structure, a tape size marker located on the main elongate tape structure indicating a number of dosing indicia on the tape, and

(Continued)

Related U.S. Application Data

(60) Continuation of application No. 14/103,353, filed on Dec. 11, 2013, now Pat. No. 9,526,850, which is a
(Continued)



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priming indicia located on the main elongate tape structure, the priming indicia being located between the dosing indicia and one end of the tape.

23 Claims, 17 Drawing Sheets**Related U.S. Application Data**

division of application No. 13/110,532, filed on May 18, 2011, now Pat. No. 8,978,966.

(60) Provisional application No. 61/417,659, filed on Nov. 29, 2010, provisional application No. 61/345,763, filed on May 18, 2010.

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See application file for complete search history.

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Final rejection dated Oct. 20, 2016 or U.S. Appl. No. 14/699,584.

Non-Final Office Action dated Jun. 24, 2016 for U.S. Appl. No. 14/713,620, 7 pages.

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Advisory Action dated Mar. 16, 2017 or U.S. Appl. No. 14/713,633.

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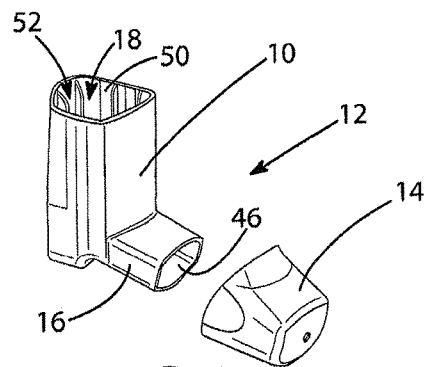


FIG. 1

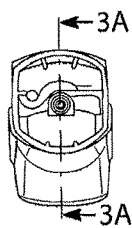


FIG. 2

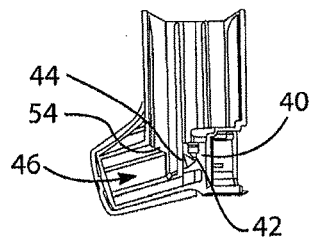


FIG. 3A

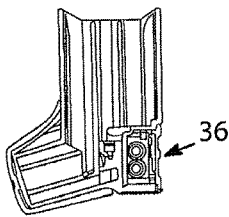


FIG. 3B

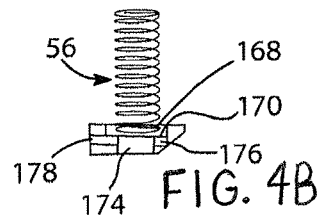


FIG. 4B

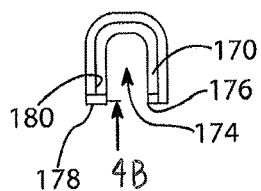


FIG. 4C

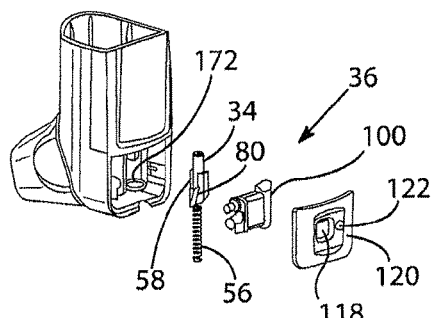


FIG. 4A

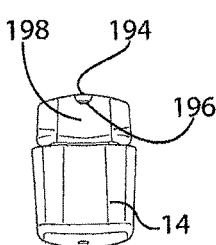


FIG. 5

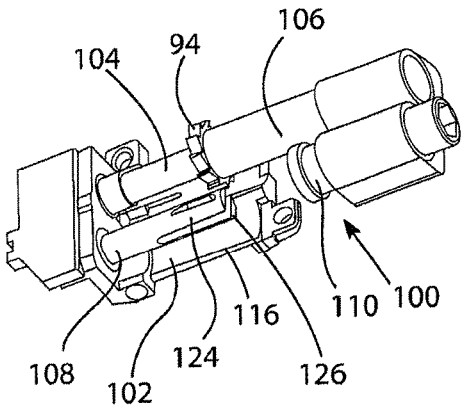


FIG. 6A

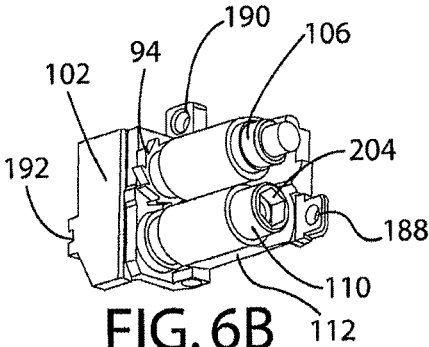


FIG. 6B

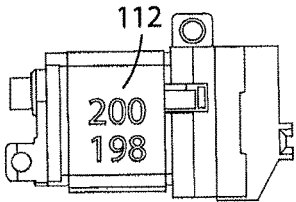


FIG. 6C

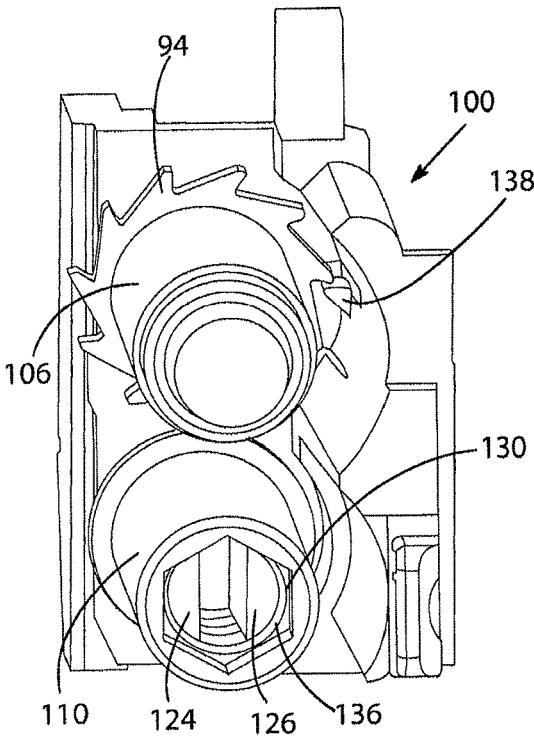


FIG. 6D

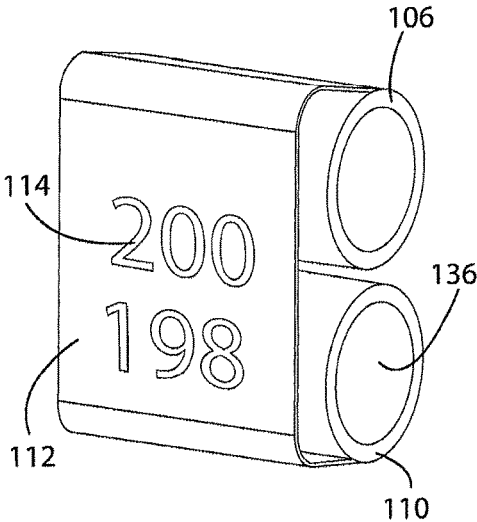


FIG. 6E

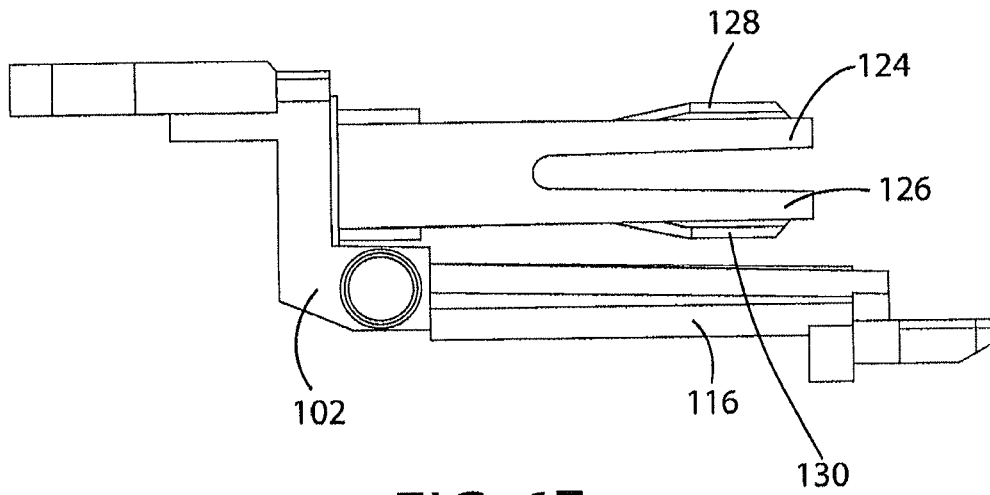


FIG. 6F

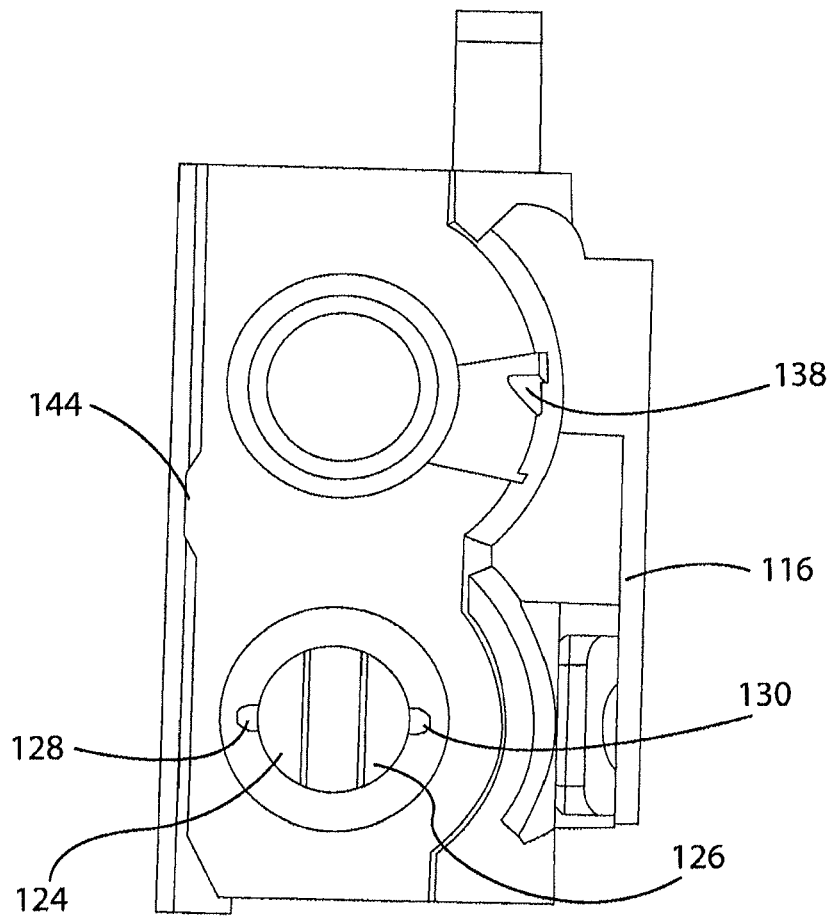


FIG. 6G

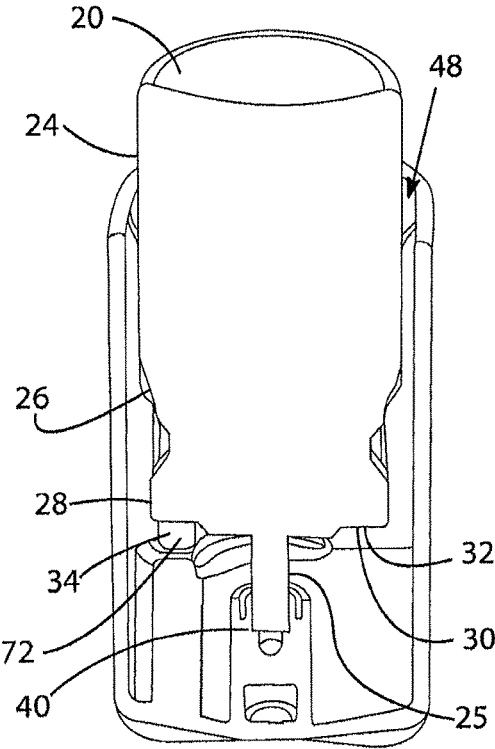


FIG. 7A

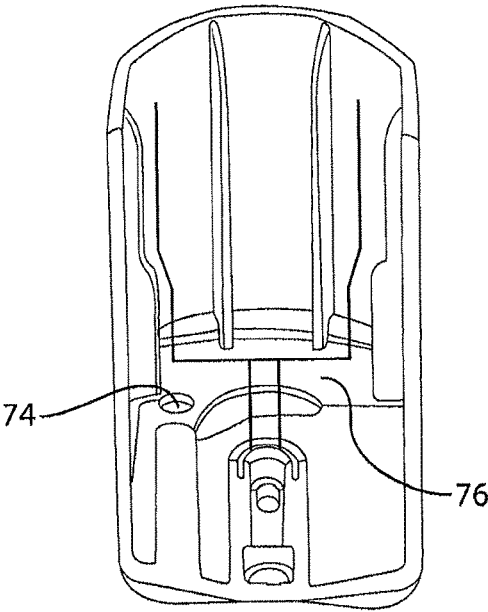


FIG. 7B

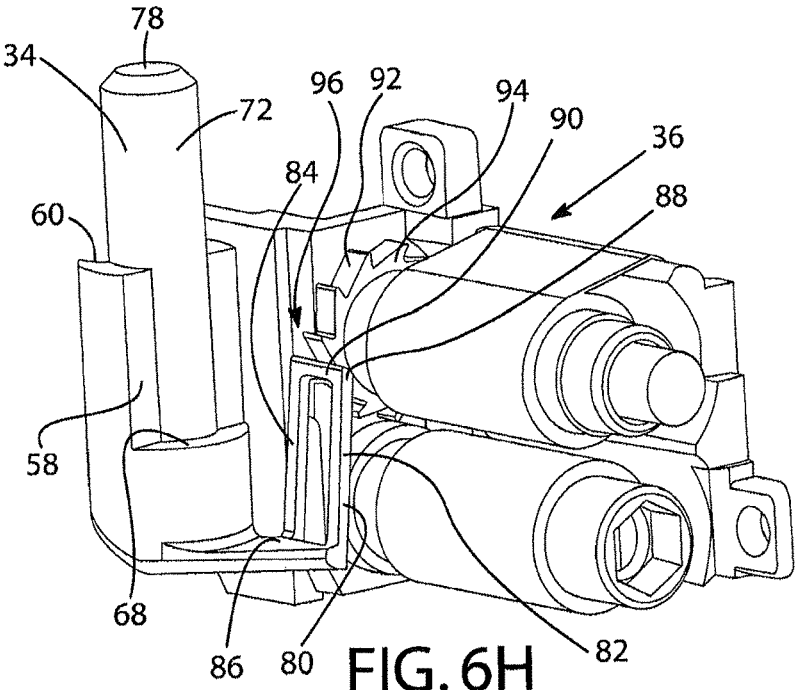
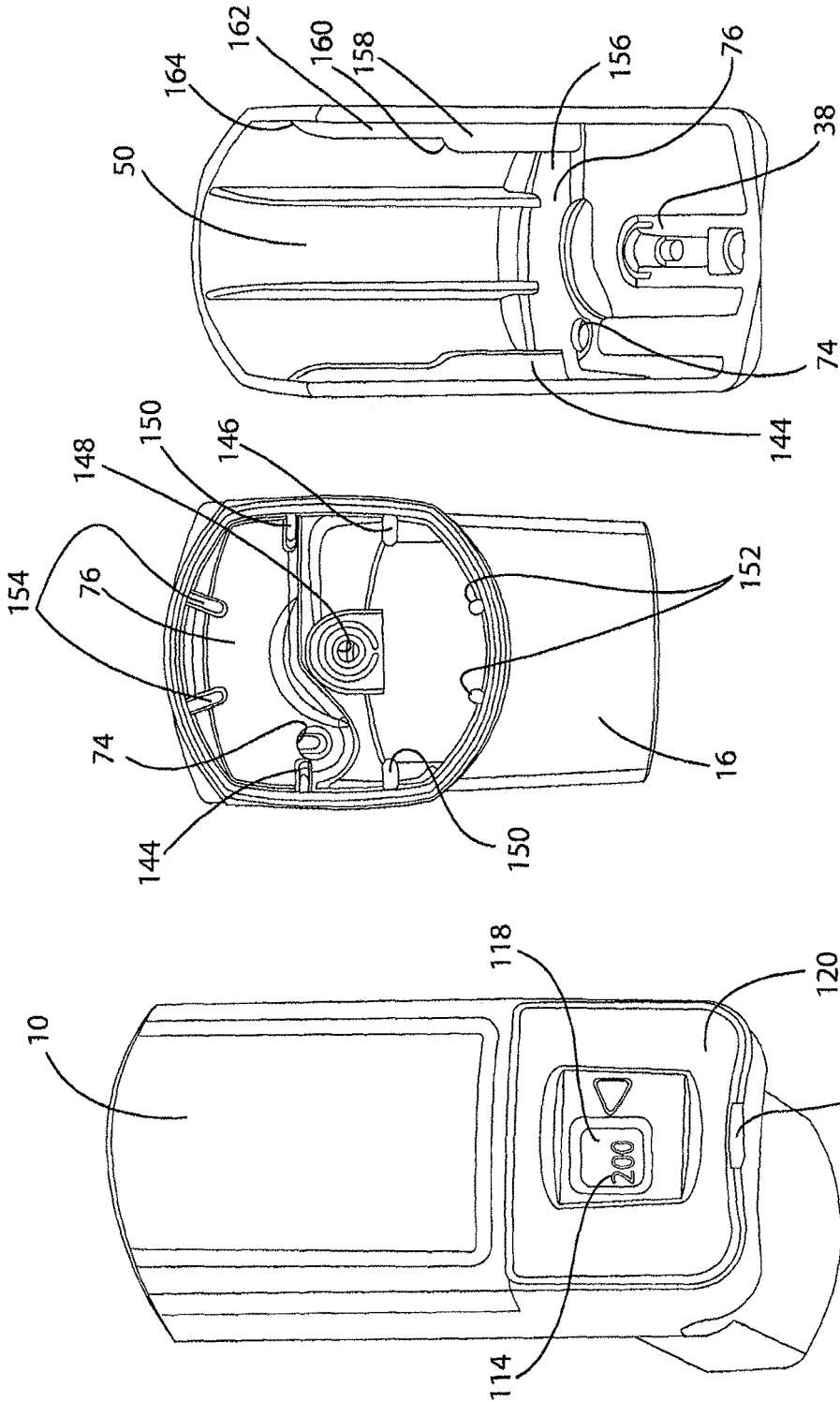


FIG. 6H



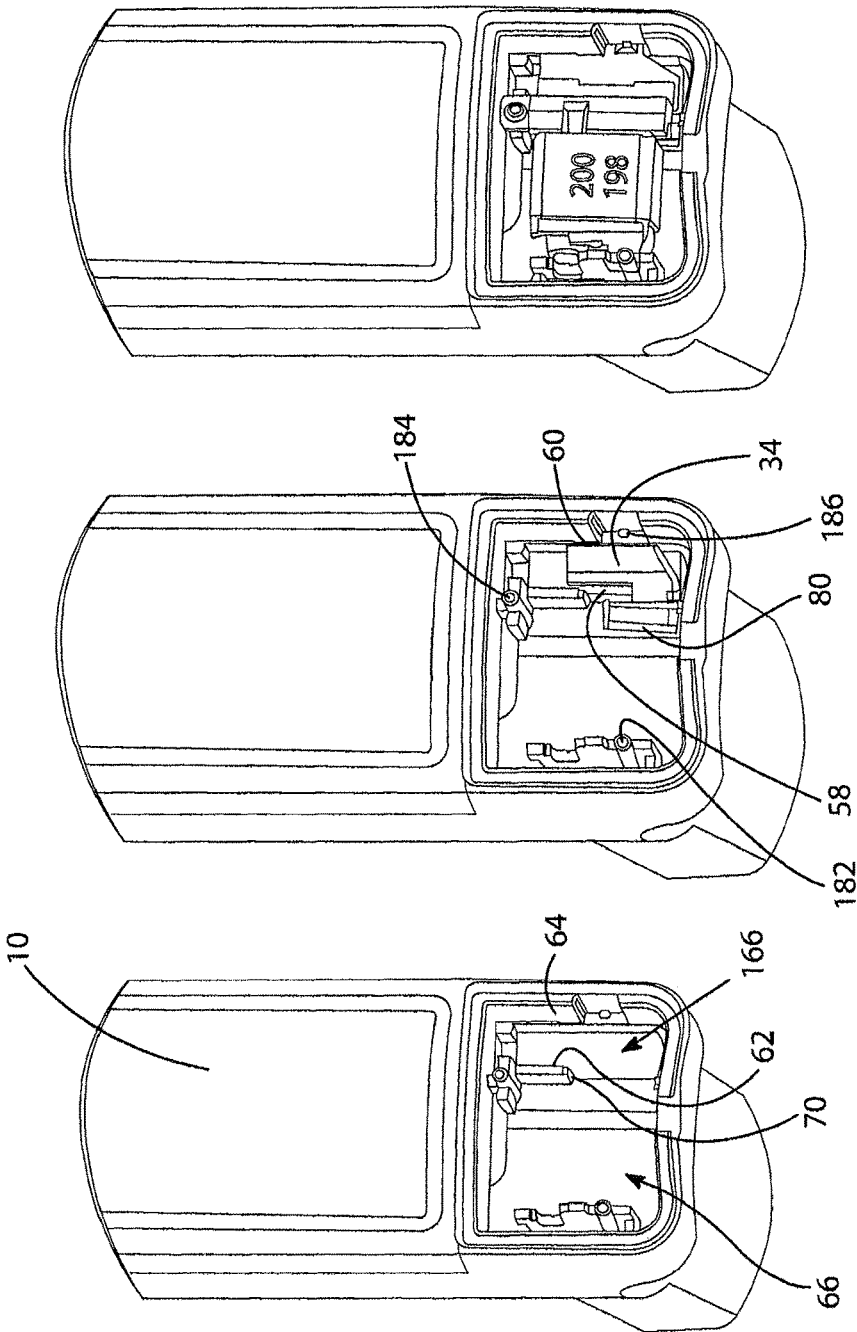


FIG. 8C

FIG. 8B

FIG. 8A

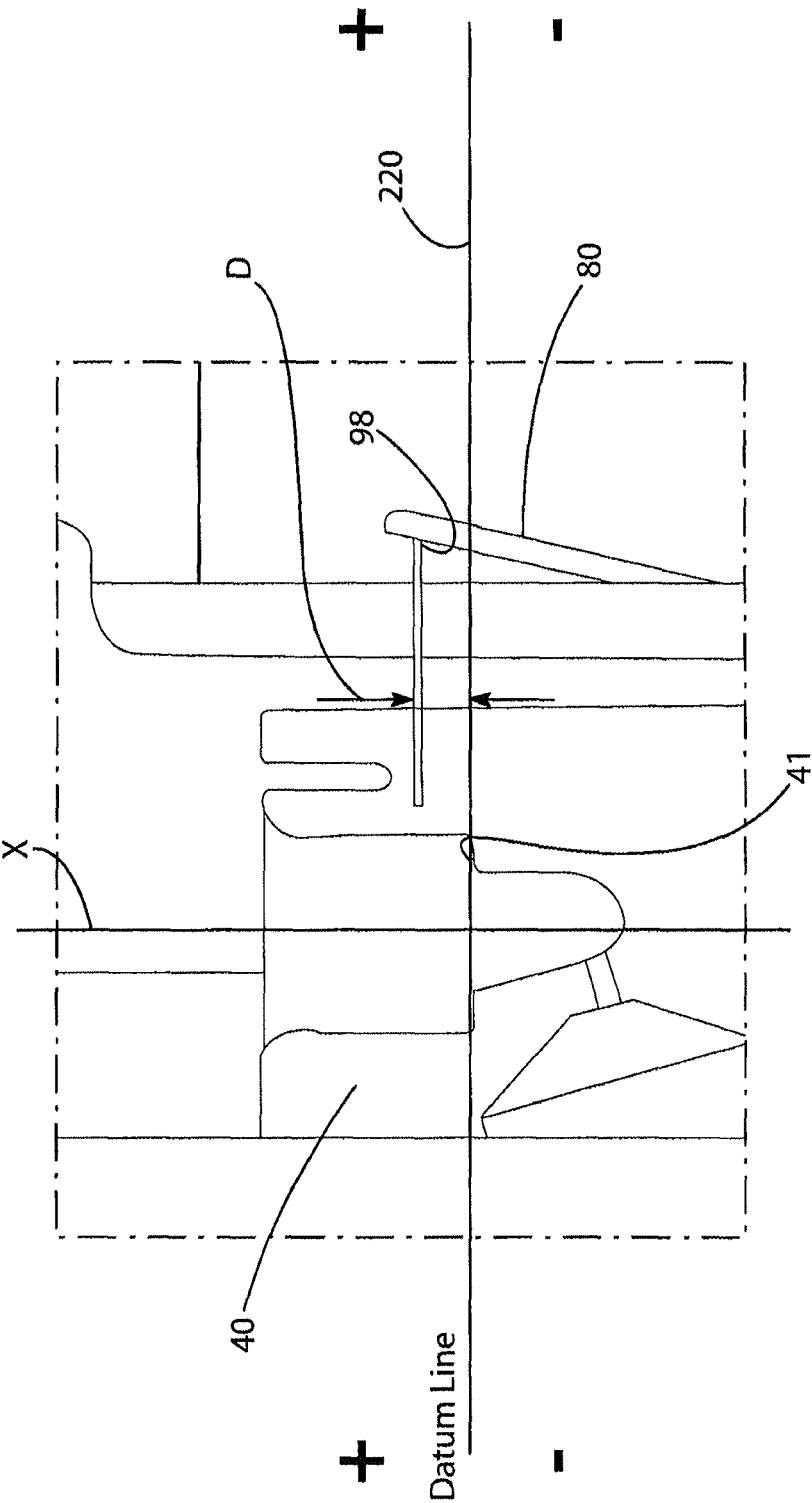
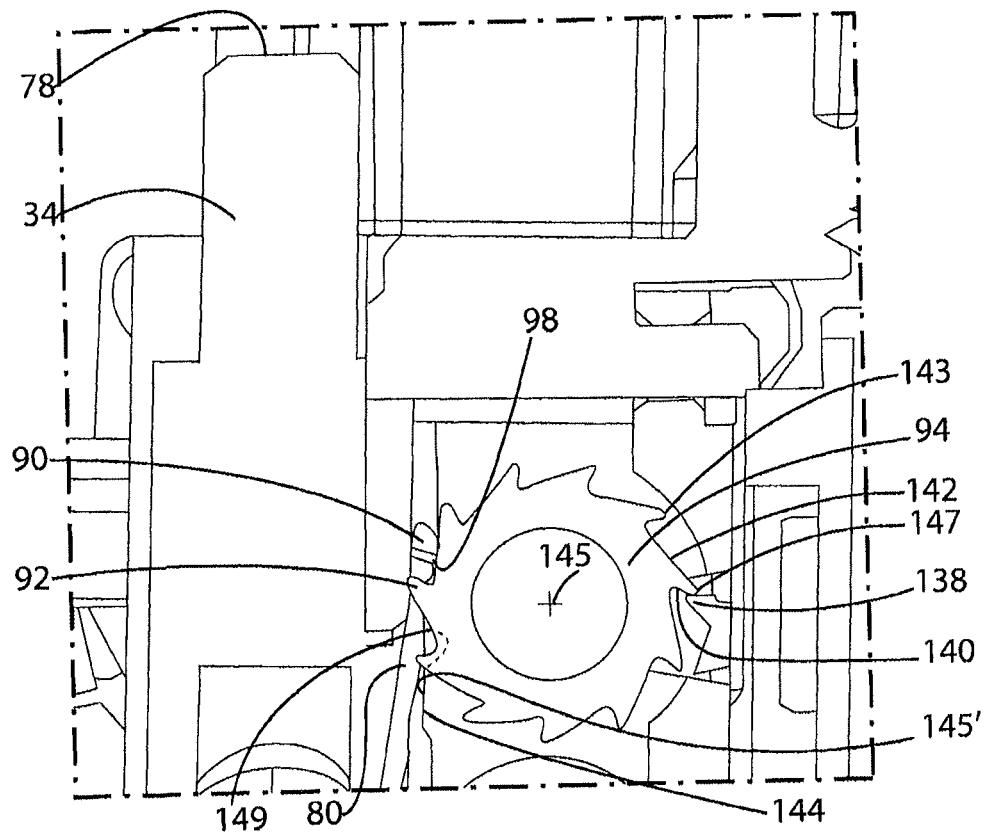
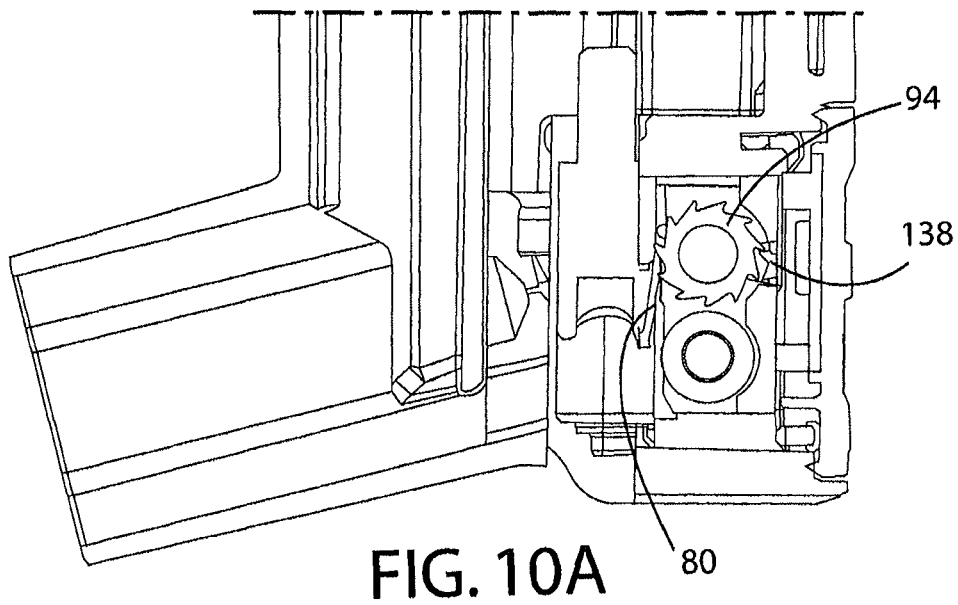


FIG. 9



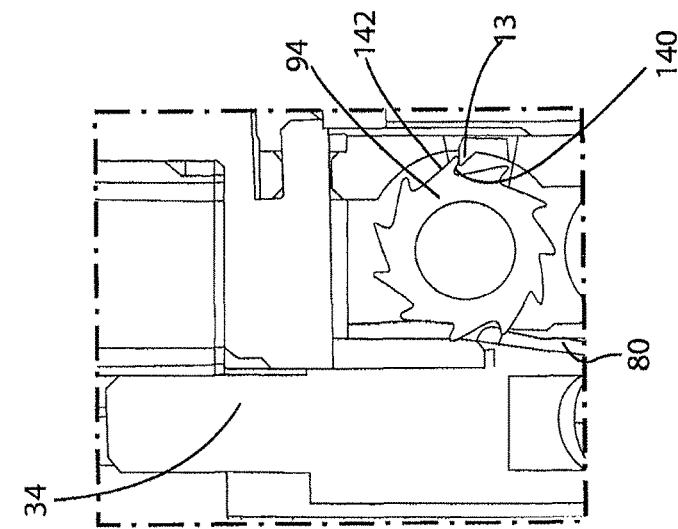


FIG. 10C

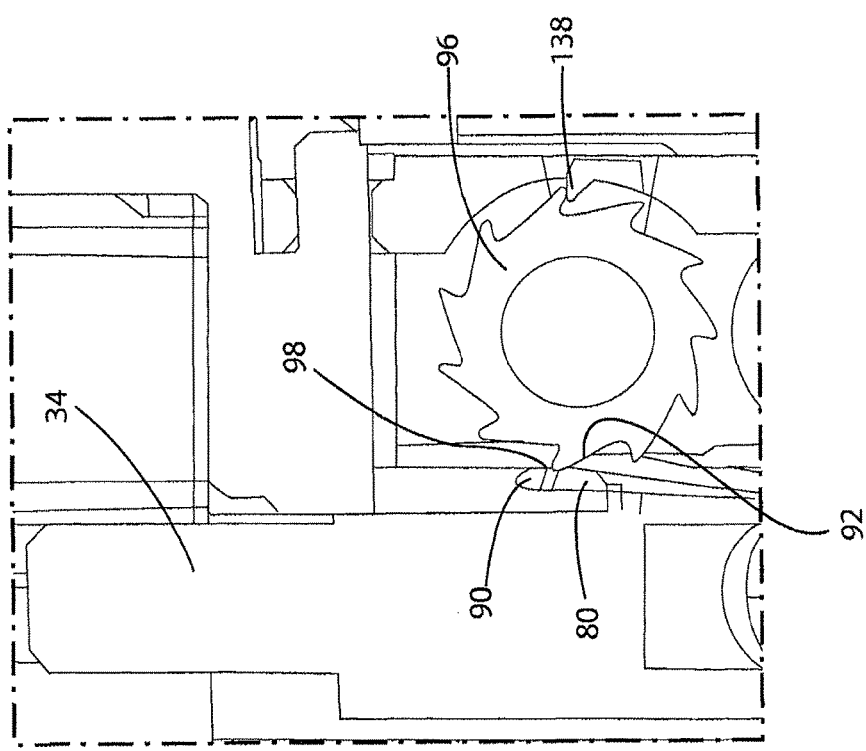


FIG. 10E

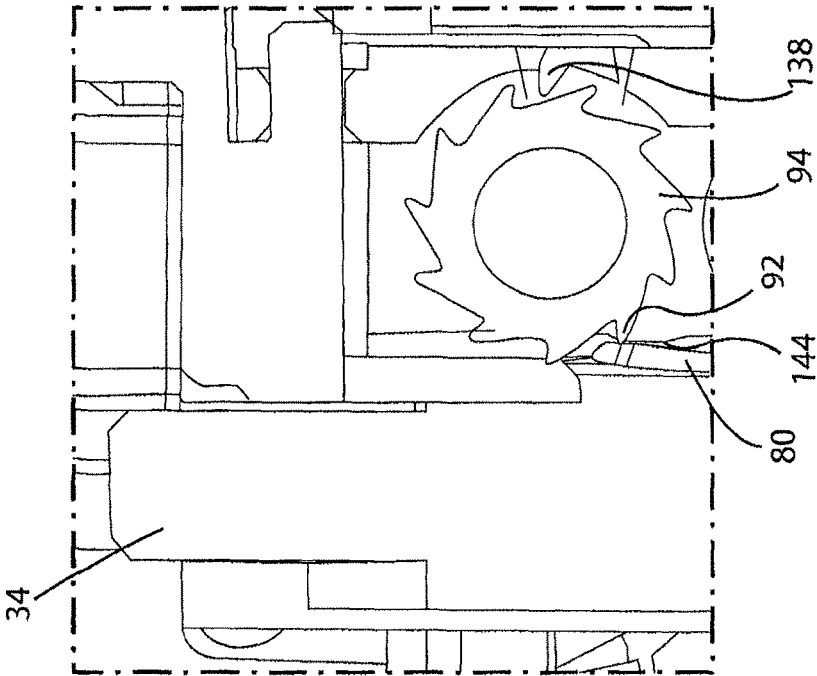


FIG. 10F

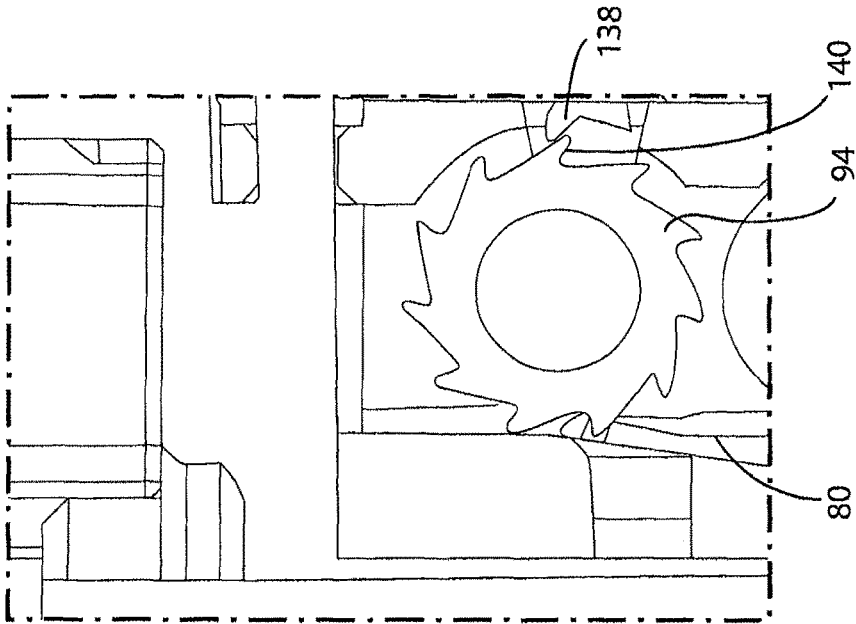


FIG. 10D

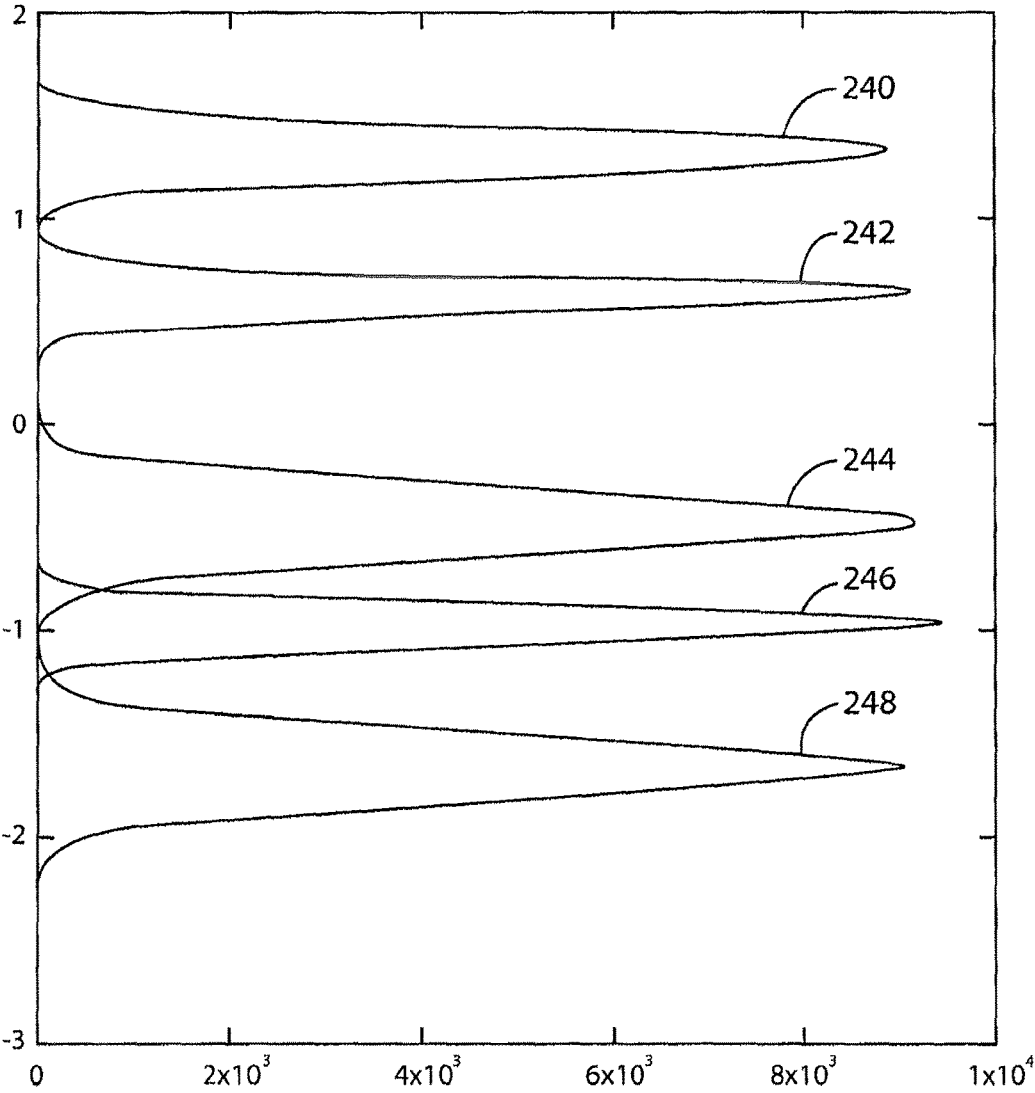


FIG. 11

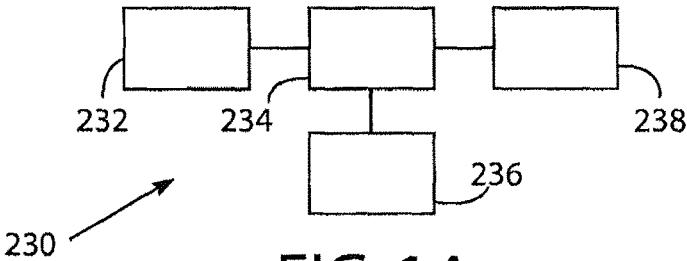


FIG. 14

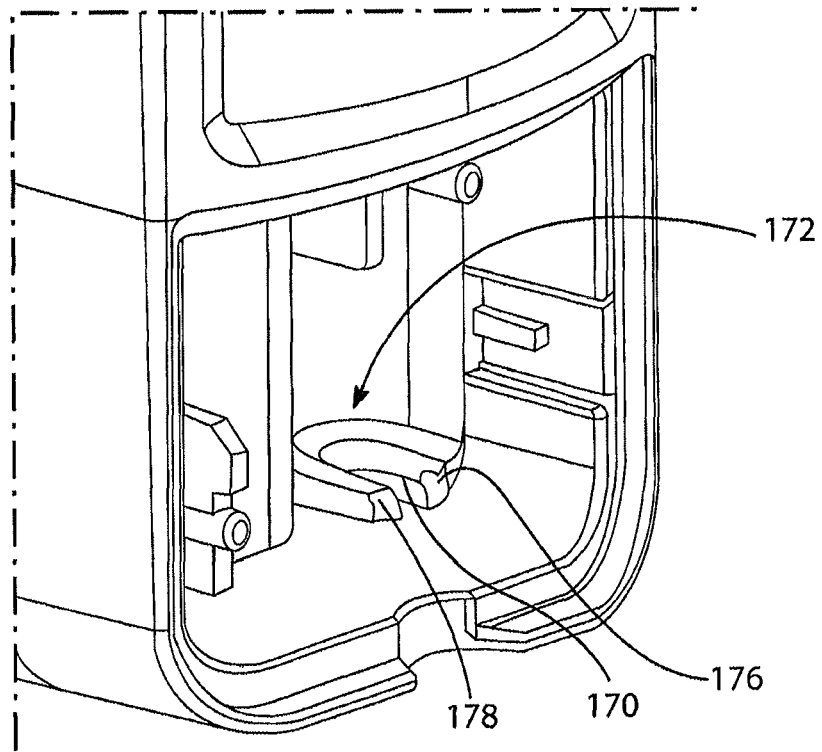


FIG. 12

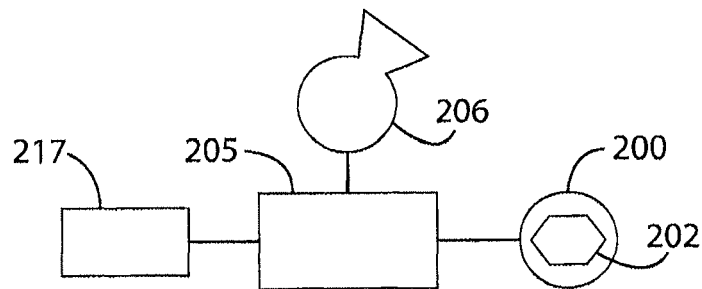
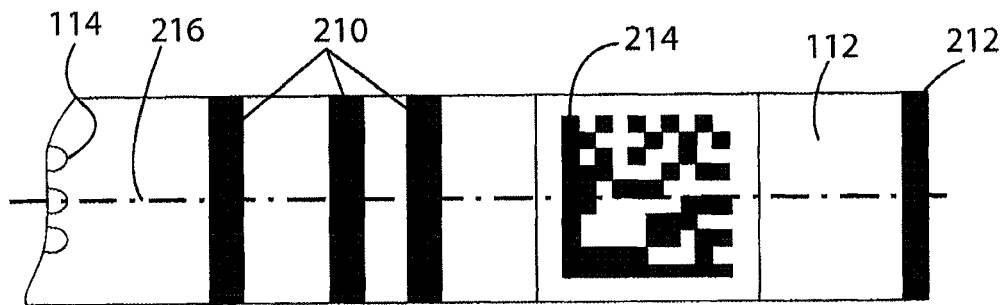


FIG. 13

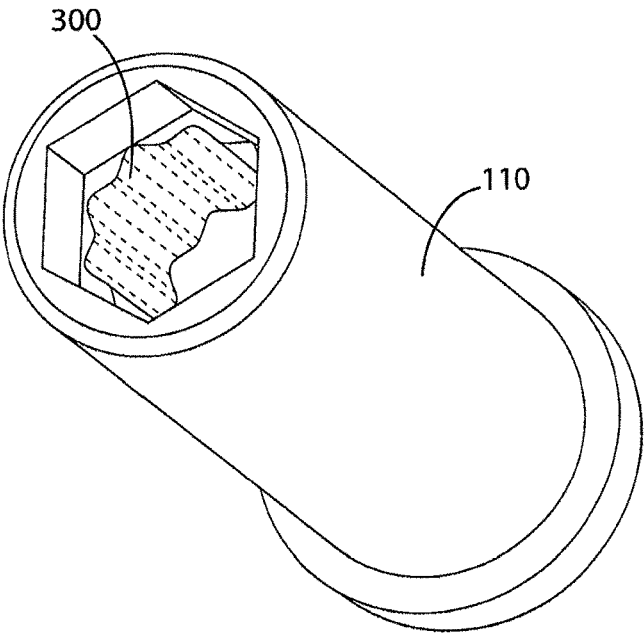


FIG. 15

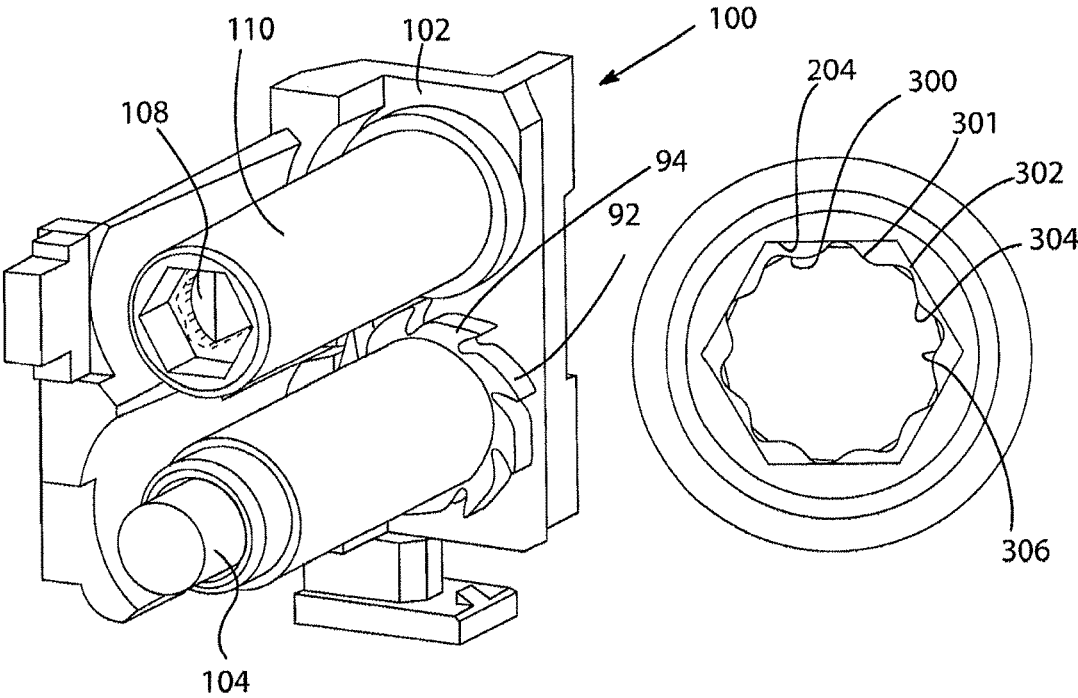


FIG. 20

FIG. 16

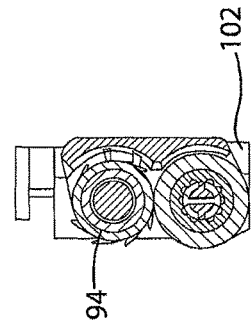


FIG. 19A

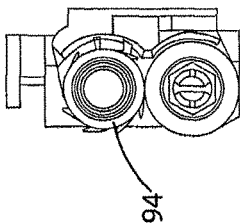


FIG. 19B

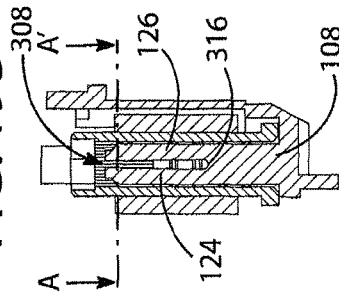


FIG. 19C

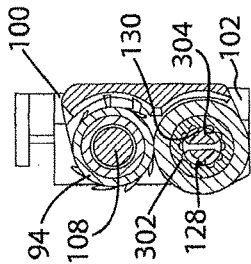


FIG. 18A

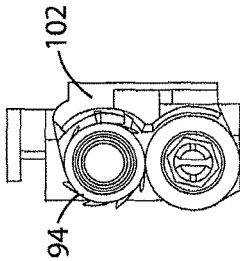


FIG. 18B

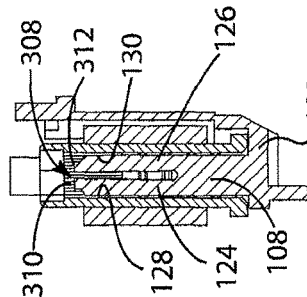


FIG. 18C

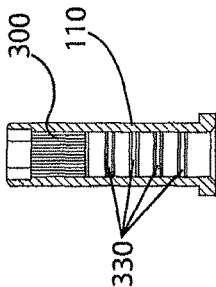


FIG. 17

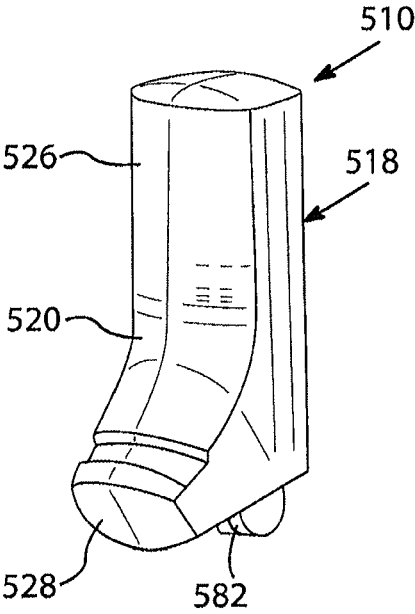


FIG. 21

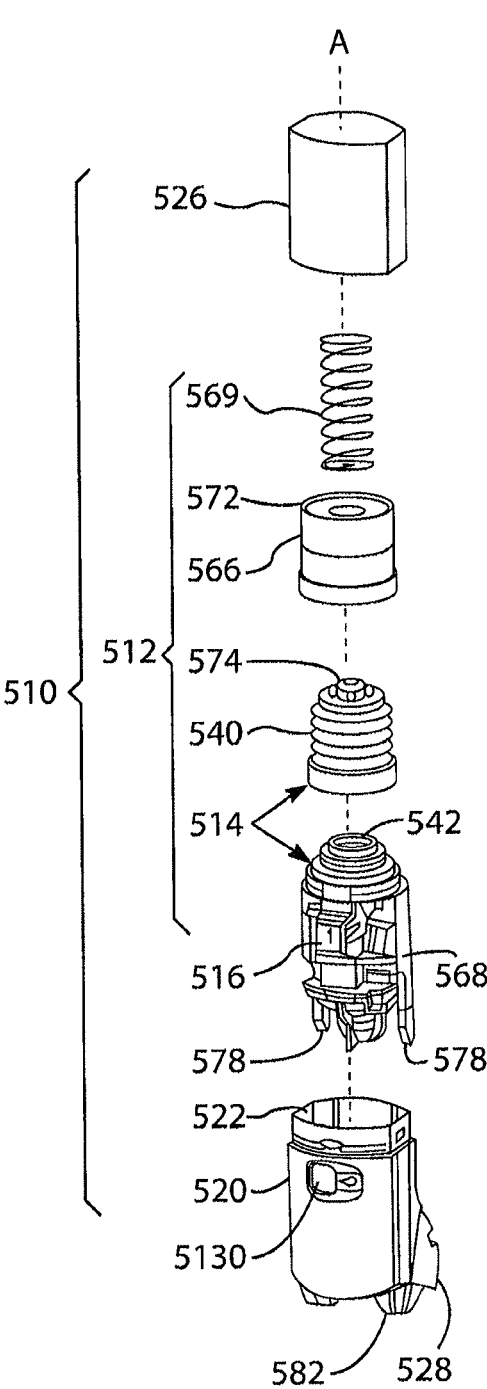


FIG. 22

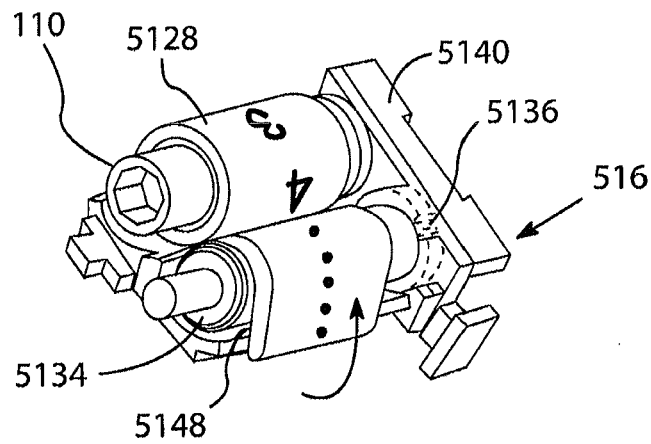


FIG. 23

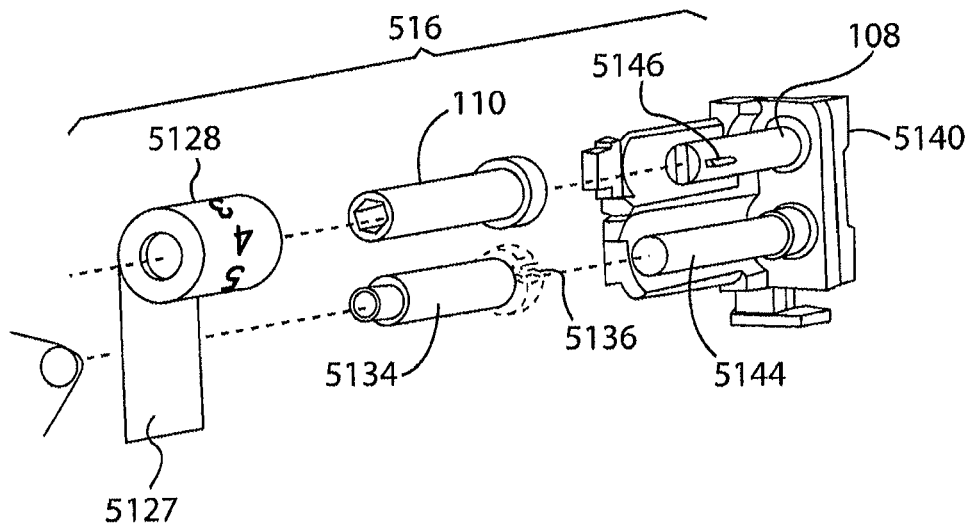


FIG. 24

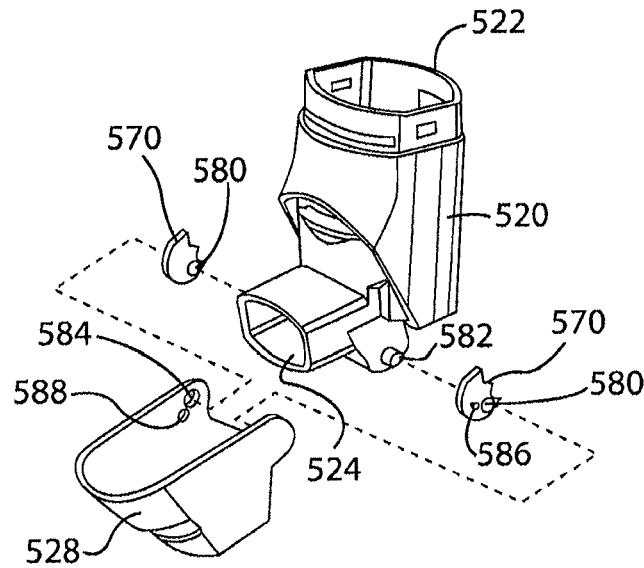


FIG. 25

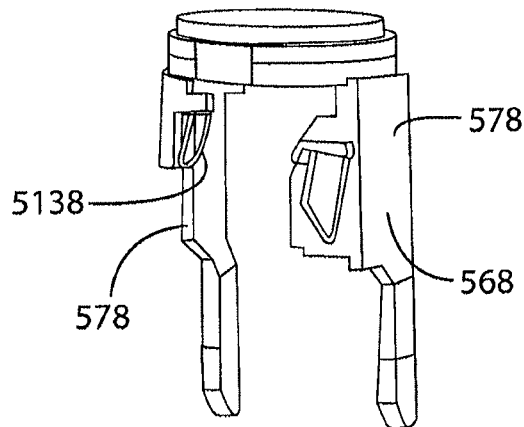


FIG. 26

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**DOSE COUNTERS FOR INHALERS,
INHALERS AND METHODS OF ASSEMBLY
THEREOF****CROSS-REFERENCE TO RELATED
APPLICATIONS**

This patent application is a continuation patent application of U.S. Non-Provisional patent application Ser. No. 14/103,353, filed Dec. 11, 2013, which is a divisional patent application of U.S. Non-Provisional patent application Ser. No. 13/110,532, filed May 18, 2011, now U.S. Pat. No. 8,978,966, issued Mar. 17, 2015, which claims priority to U.S. Provisional Patent Application No. 61/345,763, filed May 18, 2010, and U.S. Provisional Patent Application No. 61/417,659, filed Nov. 29, 2010, each of which is incorporated herein by reference in its entirety for any and all purposes.

FIELD OF THE INVENTION

The present invention relates to dose counters for inhalers, inhalers and methods of assembly thereof. The invention is particularly applicable to metered dose inhalers including dry power medicament inhalers, breath actuated inhalers and manually operated metered dose medicament inhalers.

BACKGROUND OF THE INVENTION

Metered dose inhalers can comprise a medicament-containing pressurised canister containing a mixture of active drug and propellant. Such canisters are usually formed from a deep-drawn aluminium cup having a crimped lid which carries a metering valve assembly. The metering valve assembly is provided with a protruding valve stem which, in use is inserted as a push fit into a stem block in an actuator body of an inhaler having a drug delivery outlet. In order to actuate a manually operable inhaler, the user applies by hand a compressive force to a closed end of the canister and the internal components of the metering valve assembly are spring loaded so that a compressive force of approximately 15 to 30 N is required to activate the device in some typical circumstances.

In response to this compressive force the canister moves axially with respect to the valve stem and the axial movement is sufficient to actuate the metering valve and cause a metered quantity of the drug and the propellant to be expelled through the valve stem. This is then released into a mouthpiece of the inhaler via a nozzle in the stem block, such that a user inhaling through the outlet of the inhaler will receive a dose of the drug.

A drawback of self-administration from an inhaler is that it is difficult to determine how much active drug and/or propellant are left in the inhaler, if any, especially of the active drug and this is potentially hazardous for the user since dosing becomes unreliable and backup devices not always available.

Inhalers incorporating dose counters have therefore become known.

WO 98/028033 discloses an inhaler having a ratchet mechanism for driving a tape drive dose counter. A shaft onto which tape is wound has a friction clutch or spring for restraining the shaft against reverse rotation.

EP-A-1486227 discloses an inhaler for dry powered medicament having a ratchet mechanism for a tape dose counter which is operated when a mouthpiece of the inhaler is closed. Due to the way in which the mouthpiece is opened

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and closed, and actuation pawl of the device which is mounted on a yoke, travels a known long stroke of consistent length as the mouthpiece is opened and closed.

WO 2008/119552 discloses a metered-dose inhaler which is suitable for breath-operated applications and operates with a known and constant canister stroke length of 3.04 mm+/-0.255 mm. A stock bobbin of the counter, from which a tape is unwound, rotates on a shaft having a split pin intended to hold the stock bobbin taut. However, some dose counters do not keep a particularly reliable count, such as if they are dropped onto a hard surface.

More recently, it has become desirable to improve dose counters further and, in particular, it is felt that it would be useful to provide extremely accurate dose counters for manually-operated canister-type metered dose inhalers. Unfortunately, in these inhalers, it has been found in the course of making the present invention that the stroke length of the canister is to a very large extent controlled on each dose operation by the user, and by hand. Therefore, the stroke length is highly variable and it is found to be extremely difficult to provide a highly reliable dose counter for these applications. The dose counter must not count a dose when the canister has not fired since this might wrongly indicate to the user that a dose has been applied and if done repeatedly the user would throw away the canister or whole device before it is really time to change the device due to the active drug and propellant reaching a set minimum. Additionally, the canister must not fire without the dose counter counting because the user may then apply another dose thinking that the canister has not fired, and if this is done repeatedly the active drug and/or propellant may run out while the user thinks the device is still suitable for use according to the counter. It has also been found to be fairly difficult to assembly some known inhaler devices and the dose counters therefor. Additionally, it is felt desirable to improve upon inhalers by making them easily usable after they have been washed with water.

The present invention aims to alleviate at least to a certain extent one or more of the problems of the prior art.

SUMMARY OF THE INVENTION

According to a first aspect of the present invention there is provided a dose counter for an inhaler, the dose counter having a counter display arranged to indicate dosage information, a drive system arranged to move the counter display incrementally in a first direction from a first station to a second station in response to actuation input, wherein a regulator is provided which is arranged to act upon the counter display at the first station to regulate motion of the counter display at the first station to incremental movements.

The regulator is advantageous in that it helps prevent unwanted motion of the counter display if the counter is dropped.

According to a further aspect of the present invention, the regulator provides a resistance force of greater than 0.1 N against movement of the counter display. According to still a further aspect of the present invention, the resistance force is greater than 0.3 N. According to yet a further aspect of the present invention, the resistance force is from 0.3 to 0.4 N.

Preferably, the counter comprises a tape.

Preferably, the tape has dose counter indicia displayed thereon. The first station may comprise a region of the dose counter where tape is held which is located before a display location, such as a display window, for the counter indicia.

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The first station may comprise a first shaft, the tape being arranged on the first shaft and to unwind therefrom upon movement of the counter display.

The first shaft may be mounted for rotation relative to a substantially rotationally fixed element of the dose counter.

The regulator may comprise at least one projection which is arranged on one of the first shaft and the substantially rotationally fixed element and to engage incrementally with one or more formations on the other of the first shaft and the substantially rotationally fixed element.

At least two said projections may be provided. Exactly two said projections may be provided.

Each projection may comprise a radiused surface.

The at least one projection may be located on the substantially fixed element which may comprise a fixed shaft which is fixed to a main body of the dose counter, the first shaft being rotationally mounted to the fixed shaft.

Preferably, the fixed shaft has at least two resiliently flexible legs (or forks). Each leg may have at least one said projection formed in an outwardly facing direction thereon, said one or more formations being formed on an inwardly facing engagement surface of the first shaft, said at least one projection being arranged to resiliently engage said one or more formations. Preferably, a series of said formations are provided. An even number of said formations may be provided. Eight to twelve of said formations may be provided. In one embodiment, ten said formations are provided.

Each said formation may comprise a concavity formed on an engagement surface. Each concavity may comprise a radiused surface wall portion which preferably merges on at least one side thereof into a flat wall portion surface. The engagement surface may include a series of said concavities, and convex wall portions of the engagement surface may be formed between each adjacent two said concavities, each said convex wall portion comprising a convex radiused wall portion.

Each convex radiused wall portion of each convex wall portion may be connected by said flat wall portion surfaces to each adjacent concavity.

The fixed shaft may comprise a split pin with fork legs and each projection may be located on a said fork leg.

The first shaft may comprise a substantially hollow bobbin.

Said at least one formation may be located on an inner surface of the bobbin. In other embodiments it may be located on an outer surface thereof. Said engagement surface may extend partially along said bobbin, a remainder of the respective inner or outer surface having a generally smooth journal portion along at least a portion thereof.

The drive system may comprise a tooth ratchet wheel arranged to act upon a second shaft which is located at the second station, the second shaft being rotatable to wind the tape onto the second shaft.

The second shaft may be located on a main body of the dose counter spaced from and parallel to the first shaft.

The ratchet wheel may be fixed to the second shaft is arranged to rotate therewith. The ratchet wheel may be secured to an end of the second shaft and aligned coaxially with the second shaft.

The dose counter may include anti-back drive system which is arranged to restrict motion of the second shaft. The anti-back drive system may include a substantially fixed tooth arranged to act upon teeth of the ratchet wheel.

According to a further aspect of the present invention, a dose counter includes an anti-back drive system which is arranged to restrict motion of the second shaft in a tape winding direction.

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According to a further aspect of the present invention there is provided a shaft for holding counter tape in a dose counter for an inhaler, the shaft having an engagement surface including incrementally spaced formations located around a periphery thereof, the formations comprising a series of curved concavities and convex portions.

The shaft may comprise a hollow bobbin.

The engagement surface may be a generally cylindrical inwardly directed surface.

The engagement surface may include a flat surface wall portion joining each concavity and convex wall portion.

Each concavity may comprise a radiused wall portion.

Each convex wall portion may comprise a radiused wall portion.

Said concavities may be regularly spaced around a longitudinal axis of the shaft.

Said convex wall portions may be regularly spaced around a longitudinal axis of the shaft.

In some embodiments there may be from eight to twelve said concavities and/or convex wall portions regularly spaced around a longitudinal axis thereof.

One embodiment includes ten said concavities and/or convex wall portions regularly spaced around a longitudinal axis of the shaft.

According to a further aspect of the present invention there is provided a shaft and counter tape assembly for use in a dose counter for an inhaler, the assembly comprising a rotatable shaft and a counter tape which is wound around the shaft and is adapted to unwind therefrom upon inhaler actuation, the shaft having an engagement surface which includes incrementally spaced formations located around a periphery thereof.

According to a further aspect of the present invention there is provided an inhaler for the inhalation of medication and the like, the inhaler including a dose counter as in the first aspect of the present invention.

A preferred construction consists of a manually operated metered dose inhaler including a dose counter chamber including a dose display tape driven by a ratchet wheel which is driven in turn by an actuator pawl actuated by movement of a canister, the tape unwinding from a stock bobbin during use of the inhaler, a rotation regulator being provided for the stock bobbin and comprising a wavelike engagement surface with concavities which engage against control elements in the form of protrusions on resilient forks of a split pin thereby permitting incremental unwinding of the stock bobbin yet resisting excessive rotation if the inhaler is dropped onto a hard surface.

According to another aspect of the present invention there is provided a dose counter for a metered dose inhaler having a body arranged to retain a medicament canister of predetermined configuration for movement of the canister relative thereto; the dose counter comprising: an incremental counting system for counting doses, the incremental counting system having a main body, an actuator arranged to be driven in response to canister motion and to drive an incremental output member in response to canister motion, the actuator and incremental output member being configured to have predetermined canister fire and count configurations in a canister fire sequence, the canister fire configuration being determined by a position of the actuator relative to a datum at which the canister fires medicament and the count configuration being determined by a position of the actuator relative to the datum at which the incremental count system makes an incremental count, wherein the actuator is

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arranged to reach a position thereof in the count configuration at or after a position thereof in the canister fire configuration.

This arrangement has been found to be highly advantageous since it provides an extremely accurate dose counter which is suitable for use with manually operated metered dose inhalers. It has been found that dose counters with these features have a failure rate of less than 50 failed counts per million full canister activation depressions. It has been found in the course of making the present invention that highly reliable counting can be achieved with the dose counter counting at or soon after the point at which the canister fires. It has been is covered by the present inventors that momentum and motion involved in firing the canister, and in some embodiments a slight reduction in canister back pressure on the user at the time of canister firing, can very reliably result in additional further motion past the count point.

The actuator and incremental counting system may be arranged such that the actuator is displaced less than 1 mm, typically 0.25 to 0.75 mm, more preferably about 0.4 to 0.6 mm, relative to the body between its location in the count and fire configurations, about 0.48 mm being preferred. The canister, which can move substantially in line with the actuator, can reliably move this additional distance so as to achieve very reliable counting.

The incremental count system may comprise a ratchet mechanism and the incremental output member may comprise a ratchet wheel having a plurality of circumferentially spaced teeth arranged to engage the actuator.

The actuator may comprise an actuator pawl arranged to engage on teeth of the ratchet wheel. The actuator pawl may be arranged to be connected to or integral with an actuator pin arranged to engage and be depressed by a medicament canister bottom flange. The actuator pawl may be generally U-shaped having two parallel arms arranged to pull on a central pawl member arranged substantially perpendicular thereto. This provides a very reliable actuator pawl which can reliably pull on the teeth of the ratchet wheel.

The incremental count system may include a tape counter having tape with incremental dose indicia located thereon, the tape being positioned on a tape stock bobbin and being arranged to unwind therefrom.

The actuator and incremental output member may be arranged to provide a start configuration at which the actuator is spaced from the ratchet output member, a reset configuration at which the actuator is brought into engagement with the incremental output member during a canister fire sequence, and an end configuration at which the actuator disengages from the ratchet output during a canister fire sequence.

The actuator may be arranged to be located about 1.5 to 2.0 mm, from its location in the fire configuration, when in the start configuration, about 1.80 mm being preferred.

The actuator may be arranged to be located about 1.0 to 1.2 mm, from its location in the fire configuration, when in the reset configuration, about 1.11 mm being preferred.

The actuator may be arranged to be located about 1.1 to 1.3 mm, from its location in the fire configuration, when in the end configuration, about 1.18 mm being preferred.

These arrangements provide extremely reliable dose counting, especially with manually operated canister type metered dose inhalers.

The main body may include a formation for forcing the actuator to disengage from the incremental output member when the actuator is moved past the end configuration. The formation may comprise a bumped up portion of an other-

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wise generally straight surface against which the actuator engages and along which it is arranged to slide during a canister firing sequence.

The dose counter may include a counter pawl, the counter pawl having a tooth arranged to engage the incremental output member, the tooth and incremental output member being arranged to permit one way only incremental relative motion therebetween. When the incremental output member comprises a ratchet wheel, the tooth can therefore serve as an anti-back drive tooth for the ratchet wheel, thereby permitting only one way motion or rotation thereof.

The counter pawl may be substantially fixedly mounted on the main body of the incremental count system and the counter pawl may be arranged to be capable of repeatedly engaging equi-spaced teeth of the incremental output member in anti-back drive interlock configurations as the counter is operated. The counter pawl may be positioned so that the incremental output member is halfway, or substantially halfway moved from one anti-back drive interlock configuration to the next when the actuator and incremental output member are in the end configuration thereof. This is highly advantageous in that it minimises the risk of double counting or non-counting by the dose counter.

According to a further aspect of the invention there is provided an inhaler comprising a main body arranged to retain a medicament canister of predetermined configuration and a dose counter mounted in the main body.

The inhaler main body may include a canister receiving portion and a separate counter chamber, the dose counter being located within the main body thereof, the incremental output member and actuator thereof inside the counter chamber, the main body of the inhaler having wall surfaces separating the canister-receiving portion and the counter chamber, the wall surfaces being provided with a communication aperture, an actuation member extending through the communication aperture to transmit canister motion to the actuator.

According to a further aspect of the present invention there is a provided an inhaler for metered dose inhalation, the inhaler comprising a main body having a canister housing arranged to retain a medicament canister for motion therein, and a dose counter, the dose counter having an actuation member having at least a portion thereof located in the canister housing for operation by movement of a medicament canister, wherein the canister housing has an inner wall, and a first inner wall canister support formation located directly adjacent the actuation member.

This is highly advantageous in that the first inner wall canister support formation can prevent a canister from rocking too much relative to the main body of the inhaler. Since the canister may operate the actuation member of the dose counter, this substantially improves dose counting and avoids counter errors.

The canister housing may have a longitudinal axis which passes through a central outlet port thereof, the central outlet port being arranged to mate with an outer canister fire stem of a medicament canister, the inner wall canister support formation, the actuation member and the outlet port lying in a common plane coincident with the longitudinal axis. Accordingly, this construction may prevent the canister from rocking towards the position of the dose counter actuation member, thereby minimising errors in counting.

The canister housing may have a further inner canister wall support formation located on the inner wall opposite, or substantially opposite, the actuation member. Accordingly, the canister may be supported against rocking motion away from the actuator member so as to minimise count errors.

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The canister housing may be generally straight and tubular and may have an arrangement in which each said inner wall support formation comprises a rail extending longitudinally along the inner wall.

Each said rail may be stepped, in that it may have a first portion located towards a medicine outlet end or stem block of the canister housing which extends inwardly a first distance from a main surface of the inner wall and a second portion located toward an opposite end of the canister chamber which extends inwardly a second, smaller distance from the main surface of the inner wall. This may therefore enable easy insertion of a canister into the canister housing such that a canister can be lined up gradually in step wise function as it is inserted into the canister housing.

The inhaler may include additional canister support rails which are spaced around an inner periphery of the inner wall of the canister housing and which extend longitudinally therealong.

At least one of the additional rails may extend a constant distance inwardly from the main surface of the inner wall.

At least one of the additional rails may be formed with a similar configuration to the first inner wall canister support formation.

The dose counter may, apart from said at least a portion of the actuation member, be located in a counter chamber separate from the canister housing, the actuation member comprising a pin extending through an aperture in a wall which separates the counter chamber and the canister housing.

According to a further aspect of the present invention there is provided an inhaler for inhaling medicaments having: a body for retaining a medicament store; the body including a dose counter, the dose counter having a moveable actuator and a return spring for the actuator, the return spring having a generally cylindrical and annular end; the body having a support formation therein for supporting said end of the return spring, the support formation comprising a shelf onto which said end is engageable and a recess below the shelf.

This shelf and recess arrangement is highly advantageous since it allows a tool (such as manual or mechanical tweezers) to be used to place the return spring of the actuator onto the shelf with the tool then being withdrawn at least partially via the recess.

The shelf may be U-shaped.

The support formation may include a U-shaped upstanding wall extending around the U-shaped shelf, the shelf and upstanding wall thereby forming a step and riser of a stepped arrangement.

The recess below the shelf may also be U-shaped.

At least one chamfered surface may be provided at an entrance to the shelf. This may assist in inserting the actuator and return spring into position.

A further aspect of the invention provides a method of assembly of an inhaler which includes the step of locating said end of said spring on the shelf with an assembly tool and then withdrawing the assembly tool at least partly via the recess. This assembly method is highly advantageous compared to prior art methods in which spring insertion has been difficult and in which withdrawal of the tool has sometimes accidentally withdrawn the spring again.

The cylindrical and annular end of the spring may be movable in a direction transverse to its cylindrical extent into the shelf while being located thereon.

According to a further aspect of the present invention there is provided an inhaler for inhaling medicament, the inhaler having a body for retaining a medicament store; and

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a dose counter, the dose counter having a moveable actuator and a chassis mounted on the body; the chassis being heat staked in position on the body. This is highly advantageous in that the chassis can be very accurately positioned and held firmly in place, thereby further improving counting accuracy compared to prior art arrangements in which some movement of the chassis relative to the body may be tolerated in snap-fit connections.

The chassis may have at least one of a pin or aperture heat staked to a respective aperture or pin of the body.

The chassis may have a ratchet counter output member mounted thereon.

The ratchet counter output member may comprise a ratchet wheel arranged to reel in incrementally a dose meter tape having a dosage indicia located thereon.

According to a further aspect of the present invention there is provided a method of assembling an inhaler including the step of heat staking the chassis onto the body. The step of heat staking is highly advantageous in fixedly positioning the chassis onto the body in order to achieve highly accurate dose counting in the assembled inhaler.

The method of assembly may include mounting a spring-returned ratchet actuator in the body before heat staking the chassis in place. The method of assembly may include pre-assembling the chassis with a dose meter tape prior to the step of heat staking the chassis in place. The method of assembly may include attaching a dose meter cover onto the body after the heat staking step. The cover may be welded onto the body or may in some embodiments be glued or otherwise attached in place.

According to a further aspect of the present invention there is provided an inhaler for inhaling medicament and having a body, the body have a main part thereof for retaining a medicament store; and a dose counter, the dose counter being located in a dose counter chamber of the body which is separated from the main part of the body, the dose counter chamber of the body having a dosage display and being perforated so as to permit the evaporation of water or aqueous matter in the dose counter chamber into the atmosphere.

This is highly advantageous since it enables the inhaler to be thoroughly washed and the dose counting chamber can thereafter dry out fully.

The display may comprise a mechanical counter display inside the dose counter chamber and a window for viewing the mechanical counter display. The mechanical counter display may comprise a tape. The perforated dose counter chamber may therefore enable reliable washing of the inhaler, if desired by the user, and may therefore dry out without the display window misting up.

The dose counter chamber may be perforated by a drain hole formed through an outer hole of the body. The drain hole may be located at a bottom portion of the body of the inhaler, thereby enabling full draining of the inhaler to be encouraged after washing when the inhaler is brought into an upright position.

According to a further aspect of the present invention there is provided a dose counter for an inhaler, the dose counter having a display tape arranged to be incrementally driven from a tape stock bobbin onto an incremental tape take-up drive shaft, the bobbin having an internal bore supported by and for rotation about a support shaft, at least one of the bore and support shaft having a protrusion which is resiliently biased into frictional engagement with the other of the bore and support shaft with longitudinally extending mutual frictional interaction. This arrangement may provide good friction for the bobbin, thereby improving tape counter

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display accuracy and preventing the bobbin from unwinding undesirably for example if the inhaler is accidentally dropped.

The support shaft may be forked and resilient for resiliently biasing the support shaft and bore into frictional engagement.

The support shaft may have two forks, or more in some cases, each having a radially extending protrusion having a friction edge extending therealong parallel to a longitudinal axis of the support shaft for frictionally engaging the bore of the support shaft with longitudinally extending frictional interaction therebetween.

The bore may be a smooth circularly cylindrical or substantially cylindrical bore.

Each of the above inhalers in accordance with aspects of the present invention may have a medicament canister mounted thereto.

The canister may comprise a pressurised metered dose canister having a reciprocally movable stem extending therefrom and movable into a main canister portion thereof for releasing a metered dose of medicament under pressure, for example by operating a metered dose valve inside the canister body. The canister may be operable by pressing by hand on the main canister body.

In cases in which one or more support rails or inner wall support formations are provided, the canister may at all times when within the canister chamber have a clearance of about 0.25 to 0.35 mm from the first inner wall support formation. The clearance may be almost exactly 0.3 mm. This clearance which may apply to the canister body itself or to the canister once a label has been applied, is enough to allow smooth motion of the canister in the inhaler while at the same time preventing substantial rocking of the canister which could result in inaccurate counting by a dose counter of the inhaler, especially when lower face of the canister is arranged to engage an actuator member of the dose counter for counting purposes.

According to a further aspect of the invention, a method of assembling a dose counter for an inhaler comprises the steps of providing a tape with dosing indicia thereon; providing tape positioning indicia on the tape; and stowing the tape while monitoring for the tape positioning indicia with a sensor. The method advantageously permits efficient and accurate stowing of the tape, e.g. by winding.

The dosing indicia may be provided as numbers, the tape positioning indicia may be provided as one or more lines across the tape. The stowing step comprises winding the tape onto a bobbin or shaft, and, optionally, stopping winding when the positioning indicia are in a predetermined position. The tape may be provided with pixelated indicia at a position spaced along the tape from the positioning indicia. The tape may also be provided with a priming dot.

According to a further aspect of the invention, a tape system for a dose counter for an inhaler has a main elongate tape structure, and dosing indicia and tape positioning indicia located on the tape structure. The tape positioning indicia may comprise at least one line extending across the tape structure. The tape system may comprise pixelated indicia located on the tape structure and spaced from the positioning indicia. The tape system may comprise a priming dot located on the tape structure. The positioning indicia may be located between the timing dot and the pixelated indicia. The main elongate tape structure may have at least one end thereof wound on a bobbin or shaft.

A further aspect of the invention provides a method of designing an incremental dose counter for an inhaler comprising the steps of calculating nominal canister fire and

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dose counter positions for a dose counter actuator of the inhaler; calculating a failure/success rate for dose counters built to tolerance levels for counting each fire of inhalers in which the dose counter actuators may be applied; and selecting a tolerance level to result in said failure/success rate to be at or below/above a predetermined value. This is highly advantageous in that it allows an efficient and accurate prediction of the reliability of a series of inhaler counters made in accordance with the design.

The method of designing may include selecting the failure/success rate as a failure rate of no more than one in 50 million. The method of designing may include setting an average count position for dose counters built to the tolerances to be at or after an average fire position thereof during canister firing motion. The method of designing may include setting the average count position to be about 0.4 to 0.6 mm after the average fire position, such as about 0.48 mm after. The method of designing may include setting tolerances for the standard deviation of the fire position in dose counters built to the tolerances to be about 0.12 to 0.16 mm, such as about 0.141 mm. The method of designing may include setting tolerances for the standard deviation of the count positions in dose counters built to the tolerances to be about 0.07 to 0.09 mm, such as about 0.08 mm. A further aspect of the invention provides a computer implemented method of designing an incremental dose counter for an inhaler which includes the aforementioned method of designing.

A further aspect of the invention provides a method of manufacturing in a production run a series of incremental dose counters for inhalers which comprises manufacturing the series of dose counters in accordance with the aforementioned method of designing.

A further aspect of the invention provides a method of manufacturing a series of incremental dose counters for inhalers, which comprises manufacturing the dose counters with nominal canister fire and dose count positions of a dose counter actuator relative to a dose counter chassis (or inhaler main body), and which includes building the dose counters with the average dose count position in the series being, in canister fire process, at or after the average canister fire position in the series.

According to a further aspect of the invention, the method provides fitting each dose counter in the series of incremental dose counters to a corresponding main body of an inhaler.

These aspects advantageously provide for the production run of a series of inhalers and dose counters which count reliably in operation.

According to a further aspect of the invention, an incremental dose counter for a metered dose inhaler has a body arranged to retain a canister for movement of the canister relative thereto, the incremental dose counter having a main body, an actuator arranged to be driven and to drive an incremental output member in a count direction in response to canister motion, the actuator being configured to restrict motion of the output member in a direction opposite to the count direction. This advantageously enables an inhaler dose counter to keep a reliable count of remaining doses even if dropped or otherwise jolted.

The output member may comprise a ratchet wheel. The actuator may comprise a pawl and in which the ratchet wheel and pawl are arranged to permit only one-way ratcheting motion of the wheel relative to the pawl. The dose counter may include an anti-back drive member fixed to the main body. In a rest position of the dose counter, the ratchet wheel is capable of adopting a configuration in which a back surface of one tooth thereof engages the anti-back drive member and the pawl is spaced from an adjacent back

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surface of another tooth of the ratchet wheel without positive drive/blocking engagement between the pawl and wheel.

BRIEF DESCRIPTION OF THE DRAWINGS

The present invention may be carried out in various ways and preferred embodiment of a dose counter, inhaler and methods of assembly, design and manufacture will now be described with reference to the accompanying drawings in which:

FIG. 1 is an isometric view of a main body of an embodiment of an inhaler related to the invention together with a mouthpiece cap therefor;

FIG. 2 is a top plan view of the components as shown in FIG. 1;

FIG. 3A is a section on the plane 3A-3A in FIG. 2;

FIG. 3B is a view corresponding to FIG. 3A but with a dose counter fitted to the main body of the inhaler;

FIG. 4A is an exploded view of the inhaler main body, mouthpiece cap, dose counter and a dose counter window;

FIG. 4B is a view in the direction 4B in FIG. 4C of a spring retainer of the dose counter;

FIG. 4C is a top view of the spring retainer of FIG. 4B;

FIG. 5 is a bottom view of the assembled inhaler main body, mouthpiece cap, dose counter and dose counter window;

FIGS. 6A, 6B, 6C, 6D, 6E, 6F, 6G and 6H are various views of dose counter components of the inhaler;

FIGS. 7A and 7B are sectional views showing canister clearance inside the main body of the inhaler;

FIG. 7C is a further sectional view similar to that of FIG. 7B but with the canister removed;

FIG. 7D is a top plan view of the inhaler main body;

FIGS. 8A, 8B, 8C and 8D show the inhaler main body and dose counter components during assembly thereof;

FIG. 9 shows a sectional side view of a datum line for an actuator pawl of the dose counter;

FIGS. 10A, 10B, 10C, 10D, 10E and 10F show various side views of positions and configurations of the actuator pawl, a ratchet wheel, and a count pawl;

FIG. 11 shows distributions for tolerances of start, reset, fire, count and end positions for the actuator of the dose counter;

FIG. 12 is an enlarged version of part of FIG. 4A;

FIG. 13 shows an end portion of a tape of the dose counter;

FIG. 14 shows a computer system for designing the dose counter;

FIG. 15 is an isometric view of a stock bobbin modified in accordance with the present invention for use in the dose counter of the inhaler of FIGS. 1 to 14;

FIG. 16 shows an end view of the stock bobbin of FIG. 15;

FIG. 17 is a section through a longitudinal axis of the stock bobbin of FIGS. 15 and 16;

FIGS. 18A, 18B and 18C are views of the stock bobbin of FIGS. 15 to 17 mounted in the dose counter chassis of FIGS. 1 to 14, with the control elements of the forks of the second shaft (or split pin) having a profile slightly different to that in FIG. 6F, with the forks in a compressed configuration;

FIGS. 19A, 19B and 19C are views equivalent to FIGS. 18A to 18C but with the forks in a more expanded configuration due to a different rotational position of the stock bobbin;

FIG. 20 is an isometric view of the chassis assembled and including the stock bobbin of FIGS. 15 to 17 but excluding the tape for reasons of clarity;

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FIG. 21 is a view of a preferred embodiment of a dry powder inhaler in accordance with the present invention;

FIG. 22 is an exploded view of the inhaler of FIG. 21;

FIG. 23 is a view of a dose counter of the inhaler of FIG.

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FIG. 24 is an exploded view of the dose counter shown in FIG. 23;

FIG. 25 is an exploded view of parts of the inhaler of FIG. 21; and

FIG. 26 is a view of a yoke of the inhaler of FIG. 21.

DETAILED DESCRIPTION OF THE INVENTION

FIG. 1 shows a main body 10 of a manually operated metered dose inhaler 12 in accordance with an embodiment related to the present invention and having a mouthpiece cap 14 securable over a mouthpiece 16 of the main body.

The main body has a canister chamber 18 into which a canister 20 (FIG. 7A) is slideable. The canister 20 has a generally cylindrical main side wall 24, joined by a tapered section 26 to a head portion 28 having a substantially flat lower face 30 which has an outer annular drive surface 32 arranged to engage upon and drive an actuation pin 34 of a dose counter 36 as will be described. Extending centrally and axially from the lower face 30 is a valve stem 38 which is arranged to sealingly engage in a valve stem block 40 of the main body 10 of the inhaler 12. The valve stem block 40 has a passageway 42 leading to a nozzle 44 for directing the contents of the canister 20, namely active drug and propellant, towards an air outlet 46 of the inhaler main body 12. It will be appreciated that due to gaps 48 between the canister 20 and an inner wall 50 of the main body 10 of the inhaler 12 an open top 52 of the main body 10 forms an air inlet into the inhaler 12 communicating via air passageway 54 with the air outlet 46, such that canister contents exiting nozzle 44 mix with air being sucked by the user through the air passageway 54 in order to pass together through the air outlet and into the mouth of the user (not shown).

The dose counter 36 will now be described. The dose counter 36 includes an actuation pin 34 biased upwardly from underneath by a return spring 56 once installed in the main body 10. As best shown in FIGS. 4A, 6H and 8A, the pin 34 has side surfaces 58, 60 arranged to slide between corresponding guide surfaces 62, 64 located in a dose counter chamber 66 of the main body 10, as well as an end stop surface 68 arranged to engage a corresponding end stop 70 formed in the dose counter chamber 66 to limit upward movement of the pin 34. The pin 34 has a top part 72 which is circularly cylindrical and extends through an aperture 74 formed through a separator wall 76 which separates the canister chamber 18 from the dose counter chamber 66. The top part 72 of the pin 34 has a flat top surface 78 which is arranged to engage the outer annular drive surface 32 of the canister 20.

The actuation pin 34 is integrally formed with a drive or actuator pawl 80. The actuator pawl 80 has a generally inverted U-shape configuration, having two mutually spaced and parallel arms 82, 84 extending from a base portion of the actuation pin 34, each holding at respective distal ends 88 thereof opposite ends of a pawl tooth member 90 which extends in a direction substantially perpendicular to the arms 82, 84, so as to provide what may be considered a "saddle" drive for pulling on each of the 11 drive teeth 92 of a ratchet wheel 94 of an incremental drive system 96 or ratchet mechanism 96 of the dose counter 36. As shown for example in FIG. 10B, the pawl tooth member 90 has a sharp lower

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longitudinal side edge 98 arranged to engage the drive teeth 92, the edge-to-surface contact provided by this engagement providing very accurate positioning of the actuator pawl 80 and resultant rotational positioning of the ratchet wheel 94.

The dose counter 36 also has a chassis preassembly 100 which, as shown in FIGS. 4A and 6A, includes a chassis 102 having a first shaft 104 receiving the ratchet wheel 94 which is secured to a tape reel shaft 106, and a second shaft (or split pin) 108 which is parallel to and spaced from the first shaft 104 and which slidably and rotationally receives a tape stock bobbin 110.

As shown in FIG. 6B, when the inhaler has not been used at all, the majority of a tape 112 is wound on the tape stock bobbin 110 and the tape 112 has a series of regularly spaced numbers 114 displayed therealong to indicate a number of remaining doses in the canister 20. As the inhaler is repeatedly used, the ratchet wheel 94 is rotated by the actuator pawl 80 due to operation of the actuation pin 34 by the canister 20 and the tape 112 is incrementally and gradually wound on to the tape reel shaft 106 from the second shaft 108. The tape 112 passes around a tape guide 116 of the chassis 102 enabling the numbers 114 to be displayed via a window 118 in a dose counter chamber cover 120 having a dose marker 132 formed or otherwise located thereon.

As shown in FIGS. 6A and 6D, the second shaft 108 is forked with two forks 124, 126. The forks 124, 126 are biased away from one another. The forks have located thereon at diametrically opposed positions on the second shaft 108 friction or control elements 128, 130, one on each fork. Each control element extends longitudinally along its respective fork 124, 126 and has a longitudinally extending friction surface 132, 134 which extends substantially parallel to a longitudinal axis of the second shaft and is adapted to engage inside a substantially cylindrical bore 136 inside the tape stock bobbin 110. This control arrangement provided between the bore 136 and the control elements 128, 130 provides good rotational control for the tape stock bobbin 110 such that it does not unwind undesirably such as when the inhaler is dropped. The tape force required to unwind the tape stock bobbin 110 and overcome this friction force is approximately 0.1 N.

As can be seen in FIG. 6D, as well as FIGS. 6G and 10A to 10F, the chassis 102 is provided with an anti-back drive tooth 138 or count pawl 138 which is resiliently and substantially fixedly mounted thereto. As will be described below and as can be seen in FIGS. 10A to 10F, when the actuation pin 34 is depressed fully so as to fire the metered valve (not shown) inside the canister 20, the actuator pawl 80 pulls down on one of the teeth 92 of the ratchet wheel 94 and rotates the wheel 94 anticlockwise as shown in FIG. 6D so as to jump one tooth 92 past the count pawl 138, thereby winding the tape 112 a distance incrementally relative to the dose marker 122 on the dose counter chamber 120 so as to indicate that one dose has been used.

With reference to FIG. 10B, the teeth of the ratchet wheel 94 have tips 143 which are radiused with a 0.1 mm radius between the flat surfaces 140, 142. The ratchet wheel 94 has a central axis 145 which is 0.11 mm above datum plane 220 (FIG. 9). A top/nose surface 147 of the anti-back drive tooth 138 is located 0.36 mm above the datum plane 220. The distance vertically (i.e. transverse to datum plane 220—FIG. 9) between the top nose surface 147 of the anti-back drive tooth is 0.25 mm from the central axis 145 of the wheel 94. Bump surface 144 has a lateral extent of 0.20 mm, with a vertical length of a flat 145' thereof being 1 mm, the width of the bump surface being 1.22 mm (in the direction of the axis 145), the top 149 of the bump surface 144 being 3.02

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mm vertically below the axis 145, and the flat 145' being spaced a distance sideways (i.e. parallel to the datum plane 220) 2.48 mm from the axis 145. The top surface 78 of the pin 34 (FIG. 6H) is 11.20 mm above the datum plane 220 (FIG. 9) when the actuator pawl 80 and pin 34 are in the start configuration. The length of the valve stem 22 is 11.39 mm and the drive surface 32 of the canister 20 is 11.39 mm above the datum plane 220 when the canister is at rest waiting to be actuated, such that there is a clearance of 0.19 mm between the canister 20 and the pin 34 in this configuration.

FIGS. 10A and 10B show the actuator pawl 80 and ratchet wheel 94 and count pawl 138 in a start position in which the flat top 78 of the pin 34 has not yet been engaged by the outer annular drive surface 32 of the canister 20 or at least has not been pushed down during a canister depression.

In this “start” position, the count pawl 138 engages on a non-return back surface 140 of one of the teeth 92 of the ratchet wheel 94. The lower side edge 98 of the actuator pawl is a distance “D” (FIG. 9) 1.33 mm above datum plane 220 which passes through bottom surface or shoulder 41 of valve stem block 40, the datum plane 220 being perpendicular to a main axis “X” of the main body 10 of the inhaler 12 which is coaxial with the centre of the valve stem block bore 43 and parallel to a direction of sliding of the canister 20 in the main body 10 of the inhaler 12 when the canister is fired.

As shown in FIG. 10B, an advantageous feature of the construction is that the pawl tooth/actuator 90 acts as a supplementary anti-back drive member when the inhaler 12 is not being used for inhalation. In particular, if the inhaler 12 is accidentally dropped, resulting in a jolt to the dose counter 36 then, if the wheel 94 would try to rotate clockwise (backwards) as shown in FIG. 10B, the back surface 140 of a tooth will engage and be blocked by the tooth member 90 of the pawl 80. Therefore, even if the anti-back drive tooth 138 is temporarily bent or overcome by such a jolt, undesirable backwards rotation of the wheel 94 is prevented and, upon the next canister firing sequence, the pawl 90 will force the wheel 94 to catch up to its correct position so that the dose counter 36 continues to provide correct dosage indication.

FIG. 10C shows a configuration in which the actuator pawl 80 has been depressed with the pin 34 by the canister 20 to a position in which the side edge 98 of the pawl tooth member 90 is just engaged with one of the teeth 92 and will therefore upon any further depression of the pin 34 begin to rotate the wheel 94. This is referred to as a “Reset” position or configuration. In this configuration, the lower side edge 98 of the actuator 80 is 0.64 mm above the datum plane 220.

FIG. 10D shows a configuration in which the actuator pawl 80 has been moved to a position lower than that shown in FIG. 10C and in which the metered dose valve (not shown) inside the canister has at this very position fired in order to eject active drug and propellant through the nozzle 44. It will be noted that in this configuration the count pawl 138 is very slightly spaced from the back surface 140 of the same tooth 92 that it was engaging in the configuration of FIG. 10D. The configuration shown in FIG. 10D is known as a “Fire” configuration. In this configuration the lower side edge 98 of the actuator 80 is 0.47 mm below the datum plane 220.

FIG. 10E shows a further step in the sequence, called a “Count” position in which the actuator pawl 80 has rotated the ratchet wheel 94 by the distance circumferentially angularly between two of the teeth 92, such that the count pawl 138 has just finished riding along a forward surface 142 of one of the teeth 92 and has resiliently jumped over the tooth

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into engagement with the back surface **140** of the next tooth. Accordingly, in this "Count" configuration, a sufficiently long stroke movement of the pin **34** has occurred that the tape **112** of the dose counter **36** will just have counted down one dose. In this configuration, the lower side edge **98** of the actuator is 0.95 mm below the datum plane **220**. Accordingly, in this position, the actuator **80** generally, including edge **98**, is 0.48 mm lower than in the fire configuration. It has been found that, although the count configuration happens further on than the fire configuration, counting is highly reliable, with less than 50 failed counts per million. This is at least partially due to momentum effects and to the canister releasing some back pressure on the user in some embodiments as its internal metering valve fires.

In the configuration of FIG. **10F**, the pawl **80** has been further depressed with the pin **34** by the canister **20** to a position in which it is just disengaging from one of the teeth **92** and the actuator pawl **80** is assisted in this disengagement by engagement of one of the arms **84** with a bump surface **144** on the chassis **102** (see FIG. **6G**) and it will be seen at this point of disengagement, which is called an "End" configuration, the count pawl **138** is positioned exactly halfway or substantially halfway between two of the drive teeth **92**. This advantageously means therefore that there is a minimum chance of any double counting or non-counting, which would be undesirable. In the end configuration, the side edge **98** of the actuator is 1.65 mm below the datum plane **220**. It will be appreciated that any further depression of the actuator pawl **80** and pin **34** past the "End" configuration shown in FIG. **10F** will have no effect on the position of the tape **112** displayed by the dose counter **36** since the actuator pawl **80** is disengaged from the ratchet wheel **94** when it is below the position shown in FIG. **10F**.

As shown in FIGS. **7C** and **7D**, the inner wall **50** of the main body **10** is provided with a two-step support rail **144** which extends longitudinally along inside the main body and is located directly adjacent the aperture **74**. As shown in FIG. **7B** a diametrically opposed two-step support rail **146** is also provided and this diametrically opposed in the sense that a vertical plane (not shown) can pass substantially directly through the first rail **144**, the aperture **74**, a central aperture **148** of the valve stem block **40** (in which canister stem **25** is located) and the second two-step support rail **146**. As shown in FIG. **7A** and schematically in FIG. **7B**, the rails **144**, **146** provide a maximum clearance between the canister **20** and the rails **144**, **146** in a radial direction of almost exactly 0.3 mm, about 0.25 to 0.35 mm being a typical range. This clearance in this plane means that the canister **20** can only rock backwards and forwards in this plane towards away from the actuation pin **34**. A relatively small distance and this therefore prevents the canister wobbling and changing the height of the actuation pin **34** as to undesirably alter the accuracy of the dose counter **36**. This is therefore highly advantageous.

The inner wall **50** of the main body **10** is provided with two further two-step rails **150** as well as two pairs **152**, **154** of rails extending different constant radial amounts inwardly from the inner wall **50**, so as to generally achieve a maximum clearance of almost exactly 0.3 mm around the canister **20** for all of the rails **144**, **146**, **150**, **152**, **154** spaced around the periphery of the inner wall **50**, in order to prevent undue rocking while still allowing canister motion freely inside the inhaler **12**. It will be clear from FIG. **7C** for example that the two-step rails have a first portion near an outlet end **156** of the canister chamber **18**, the first portion having a substantially constant radial or inwardly-extending width, a first step **160** leading to a second portion **162** of the rail, the

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second portion **102** having a lesser radial or inwardly extending extent than the first portion **156**, and finally a second step **164** at which the rail merges into the main inner wall **50** main surface.

A method of assembling the inhaler **12** will now be described.

With reference to FIG. **8A**, the main body **10** of the inhaler **12** is formed by two or more plastics mouldings which have been joined together to the configuration shown.

As shown in FIG. **8B**, the actuator pawl **80** and pin **34** are translated forward into position into a pin receiving area **166** in the dose counter chamber **66** and the pin **34** and actuator **80** may then be raised until the pin **34** emerges through the aperture **74**.

Next, the return spring **56** may be inserted below the pin **34** and a generally cylindrical annular lower end **168** of the spring **56** may be moved by a tweezer or tweezer-like assembly tool (not shown) into engagement with a shelf **170** of a spring retainer **172** in the dose counter chamber **66**. The spring retainer **172** is U-shaped and the shelf **170** is U-shaped and has a recess **174** formed below it. As shown in FIGS. **4B**, **4C** and **12** shelf **170** includes three chamfer surfaces **176**, **178**, **180** arranged to assist in moving the lower end of the spring **168** into position onto the shelf using the assembly tool (not shown). Once the lower end of the spring **168** is in place, the assembly tool (not shown) can easily be removed at least partly via the recess **174** below the lower end **168** of the spring **56**.

The tape **112** is attached at one end (not shown) to the tape stock bobbin **110** and is wound onto the bobbin by a motor **200** (FIG. **13**) having a hexagonal output shaft **202** which engages in a hexagonal socket **204** (FIG. **6B**) of the bobbin. During winding, the tape is monitored by a sensor **206**, which may be in the form of a camera or laser scanner, which feeds data to a computer controller **205** for the motor **200**. The controller **205** recognises three positioning markers **210** in the form of lines across the tape **112** and stops the motor **202** when the tape **112** is nearly fully wound onto the bobbin **110**, such that the distal end **212** of the tape **112** can be secured, e.g. by adhesive, to the tape reel shaft **106**. The controller **205** also recognises a pixelated tape size marker **214** observed by the sensor **206** and logs in a stocking system data store **217** details of the tape **112** such as the number of numbers **114** on the tape, such as one hundred and twenty or two hundred numbers **114**. Next, the tape reel shaft is wound until an appropriate position of the lines **210** at which a priming dot **216** will, once the bobbin **110** and reel shaft **106** are slid onto the second shaft **108** and second shaft **104**, be in a position to be located in the window **118** when the inhaler **12** is fully assembled. In the embodiments, the bobbin **110** and reel shaft **106** may be slid onto the shafts **108**, **104** before the tape **112** is secured to the reel shaft **106** and the reel shaft may then be wound to position the priming dot **216**.

Next, the assembled dose counter components of the chassis preassembly **100** shown in FIG. **6B** may as shown in FIG. **8C** be inserted into the dose counter chamber **66**, with pins **182**, **184**, **186** formed on the main body **10** in the dose counter chamber **66** passing through apertures or slots **188**, **190**, **192** formed on the chassis **102**, such that the pins **182**, **184**, **186** extend through (or at least into) the apertures or slots **188**, **190**, **192**. With the chassis **102** being relatively firmly pushed towards the main body **10**, the pins **182**, **184**, **186** are then heat staked and the chassis **102** is therefore after this held very firmly in position in the main body and is unable to move, thereby assisting in providing great accuracy for the dose counter **36**. Next, as shown in FIG. **8D**, the

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dose counter chamber cover **120** may be fitted over the dose counter chamber **66** and may be secured in place such as by welding, with the priming dot **216** being displayed through the window.

The user can, when readying the inhaler **12** for first use, prime the inhaler by depressing the canister **20** three times which will bring the first number **114** on the tape into display through the window **118** in place of the priming dot **216**, the number **114** shown in FIG. **8D** being “200”, thereby indicating that 200 doses are remaining to be dispensed from the canister **20** and inhaler **12**.

As shown in FIG. **8D**, and in FIG. **5**, an open drain hole **194** is provided at the bottom of the dose counter chamber **66** by a substantially semi-circular cut-out or recess formation **196** in a lower surface **198** of the main body **10** of the inhaler. Accordingly, if the user (not shown) should decide to wash the main body **10** of the inhaler, for example after encountering an unhygienic situation or simply as a matter of choice, the drain hole **194** allows initial draining of water from inside the dose counter chamber **66** and also thereafter evaporation of water or any aqueous matter in the dose counter chamber **66** so that the window **118** does not mist up undesirably.

FIG. **14** shows a computer system **230** for designing the dose counter **36** and in particular for calculating distributions representative of average positions and standard deviations in a production series of inhalers of the start, reset, fire, count and end positions of the actuator lower side edge **98** relative to the datum plane **220** (FIG. **9**) and therefore of the actuator pawl **80** generally relative to the ratchet wheel **94**, chassis **102** and, when the inhaler **12** is fully assembled, the main body **10** of the inhaler **12**. The computer system **230** includes a data store **232**, a CPU **234**, an input device **236** (such as a keyboard or communication port) and an output device **238** (such as a communications port, display screen and/or printer). A user may enter data via the input device **236** which may be used by the CPU **234** in a mathematical calculation to predict count failure rates when the various dose counters are to be built in a series with dose counter positions set with given averages and standard deviations and taking into account any momentum/inertia effects and metering valve user-back-pressure reduction effect which will occur upon canister firing of a given type of canister. The computer system **230** is thus mathematically used to design the distributions. For the inhaler **12** described herein with the dose counter **36** and canister **20**, the distributions are designed as shown in FIG. **11**. The x axis shows distance of the lower side surface **98** of the actuator **80** above the datum plane **220** and the y axis is representative of the distribution. Thus, curve **240** shows that the start configuration has an average 1.33 mm above the datum plane **200** (standard deviation is 0.1 mm), curve **242** shows that the reset configuration has an average of 0.64 mm above the datum plane **220** (standard deviation is 0.082 mm), curve **244** shows the fire configuration has an average 0.47 mm below the datum plane **220** (standard deviation is 0.141 mm), curve **246** shows the count configuration has an average 0.95 mm below the datum plane **220** (standard deviation is 0.080 mm), and curve **248** shows the end configuration has an average of 1.65 mm below the datum plane **220** (standard deviation is 0.144 mm).

FIGS. **15** to **20** show a version of the inhaler modified in accordance with the present invention. In these drawings, the same reference numerals have been used to those in the earlier drawings to denote the equivalent components. The inhaler **12** is the same as that in FIGS. **1** to **14** apart from the following modifications.

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First, it can be seen that there is a modification in that the drive teeth **92** of the ratchet wheel **94** have a different profile to that in FIGS. **1** to **14**. There are also only nine ratchet teeth **94** in this embodiment instead of eleven.

Additionally, as shown in FIGS. **18C** and **19C**, the control elements **128**, **130** on the forks **124**, **126** of the second shaft **108** have a tapered profile which is different to the profile of the control elements **128**, **130** shown in FIG. **6F**. Either profile can be used in the embodiment of FIGS. **15** to **20** however.

Furthermore, as shown in FIG. **15**, the tape stock bobbin **110** has an inwardly facing generally cylindrical engagement surface **300** with a wavelike form extending partially therealong. The engagement surface **300** has a cross-section **301** perpendicular to the longitudinal length of the stock bobbin **110** which is constant therealong. This cross-section **301** can be seen in FIG. **16** and consists of a series of ten regularly spaced concavities **302** and ten convex wall portions **304**. The convex wall portions **304** are equi-spaced between the concavities **302**. Each concavity **302** has a radius of 0.2 mm. Each convex wall portion **304** also has a radius of 0.2 mm. Finally, the cross section **301** also includes flat wall portions **306** between all of the radiused wall portions of the concavities **302** and convex wall portions **304**. The geometry of the cross-section **301** is therefore defined by the radii of the concavities **302** and convex wall portions **304**, the flat wall portions **306** and the fact that there are ten concavities **302** and convex wall portions **304**.

The minor diameter of the engagement surface **300**, i.e. between the tips of opposite convex wall portions **304**, is 2.46 mm. The major diameter of the engagement surface **300**, i.e. between the outermost portions of the concavities **302**, is 2.70 mm. The undeformed tip to tip maximum diameter of the forks **124**, **126** of the split pin (the second shaft) **108**, i.e. in the region of the maximum radio extent of the control elements **128**, **130**, is 3.1 millimeters and it will therefore be appreciated that the forks **124**, **126** are resiliently compressed once the stock bobbin **110** has been assembled onto the split pin **108** in all rotational configurations of the stock bobbin **110** relative to the split pin **108**. The minimum gap between the forks **124**, **126** in the plane of the cross sections of FIGS. **18C** and **19C** is 1 mm when the split pin **108** is in the undeformed, pre-inserted state. When the split pin **108** is at maximum compression, as shown in FIGS. **18A** to **18C** when the control elements **128**, **130** are shown to be engaged on top of the convex wall portions **304**, the gap **308** between the tips **310**, **312** of the forks **124**, **126** is 0.36 mm. On the other hand, when the split pin **108** is at minimum compression (once inserted into the stock bobbin) as shown in FIGS. **19A** to **19C**, when the control elements **128**, **130** rest in the concavities **302**, the gap between the tips **310**, **312** of the forks **124**, **126** is 0.6 mm. The control elements **128**, **130** are outwardly radiused with a radius also of 0.2 mm such that they can just rest on the concavities **302** with full surface contact (at least at an axial location on the split pin where the tapered control elements are at their maximum radial extent), without rattling in, locking onto or failing to fit in the concavities **302**. The radii of the control elements **128**, **130** is therefore preferably substantially the same as the radii of the concavities **302**.

It will be appreciated that whereas FIGS. **18B** and **19B** are end views along the coaxial axis of the stock bobbin **110** and split pin **108**, FIGS. **18A** and **19A** are cross-sections. FIG. **19A** is a section on the plane A-A' in FIG. **19C** and FIG. **18A** is a section at the same plane, but of course with the stock bobbin **110** rotated relative to the split pin **108**.

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As the inhaler 12 is used and the ratchet wheel 94 rotates in order to count used doses, the stock bobbin rotates incrementally through rotational positions in which rotation is resisted, i.e. due to increasing compression of the split pin 108 at such rotational positions, and rotational positions in which rotation is promoted, i.e. due to decreasing compression of the split pin 108 at such rotational positions and this may involve a click forward of the stock bobbin 110 to the next position equivalent to that in FIGS. 19A to 19C in which the control elements 128, 130 of the split pin art located in the concavities 302. This functionality firstly allows the stock bobbin to unwind during use as required, but also prevents the tape 112 from loosening during transit if the inhaler 12 is dropped, such as onto a hard surface. This is highly advantageous, since the tape 11 is prevented from moving to a position in which it will give an incorrect reading regarding the number of doses in the canister.

During compression and expansion of the forks in the radial direction between the two configurations shown in FIGS. 18C and 19C, the forks 124, 126 rotate about a point 316 on the split pin where the forks 124, 126 come together. This rotational action means that there is a camming action between the forks 124, 126 and the engagement surface 300 without significant friction but, nevertheless, the resilient forces provided by the regulator formed by the engagement surface 300 and forks 124, 126 are able to regulate unwinding of the tape such that it does not easily occur during transit or if the inhaler 12 is dropped. It has been found during testing that a force of 0.3 to 0.4 N needs to be applied to the tape 112 to overcome the regulator at the stock bobbin 110. 0.32 N is achieved with the control elements 128 having the profile shown in FIG. 19C and 0.38 N is achieved with the profile of the control elements 128 altered to be as shown as described with reference to FIG. 6F. These forces are substantially higher than the 0.1 N force mentioned above and undesirable movement of the tape is substantially avoided even if the inhaler is dropped onto a hard surface. The modified arrangement of FIGS. 15 to 20 does not provide this force "constantly" such that there is overall not an undesirably high friction of the tape 112 as it passes over the other components of the dose counter because, due to the incremental nature of the resilient forces at the regulator, the tape 112 can incrementally relax as it slides over the stationary chassis components.

Instead of having ten concavities 302 and convex wall portions 304, other numbers may be used, such as 8 or 12. However, it is preferred to have an even number, especially since two control elements 128, 130 are provided, so that all of the control elements 128, 130 will expand and contract simultaneously. However, other arrangements are envisaged with 3 or more forks and the number of concavities/convex wall portions may be maintained as an integer divisible by the number of forks to maintain a system with simultaneous expansion/contraction. For example, the use of 9, 12 or 15 concavities/convex wall portions with 3 forks is envisaged.

Instead of having the engagement surface 300 on the inside of the stock bobbin 110, it could be placed on the outside of the stock bobbin 110 so as to be engaged by flexible external legs/pawls or similar.

It will be noted that the regulator provided by the engagement surface 300 and forks 124, 126 does not only allow rotation of the stock bobbin in one direction as is the case with the ratchet wheel 94. Rotation in both directions is possible, i.e. forwards and backwards. This means that during assembly, the stock bobbin 110 can be wound backwards during or after fitting the bobbin 100, shaft 106 and tape 112 onto the carriage 102, if desired.

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The stock bobbin 110 and the carriage 102 including the split pin 108 are both moulded of polypropylene material.

It will be seen from FIG. 16 that the cross-sectional shape 301 is not symmetrical within the hexagonal socket 204. This has enabled the hexagonal socket 204 to be maintained at a useful size while still allowing the desired size and geometry of the cross section 301 to fit without interfering with the hexagonal shape of the hexagonal socket 204 and also permits moulding to work during manufacture.

As shown in FIG. 17, the stock bobbin 110 has a series of four circumferential ribs 330 inside it and a spaced therealong. These hold the stock bobbin 110 on the correct side of the mould tool during moulding.

FIGS. 21 and 22 show a preferred embodiment in accordance with the invention of an inhaler 510 for dispensing a dry-powdered medicament in metered doses for patient inhalation. The inhaler 510 is as disclosed in FIGS. 1 to 16 or EP-A-1330280, the contents of which are hereby fully incorporated herein by reference, but with the stock bobbin 110 and second shaft 108 of the dose counter 516 modified so as to be as in FIGS. 15 to 20 hereof. Thus, the dry powder inhaler 510 generally includes a housing 518, and an assembly 512 received in the housing (see FIG. 21). The housing 518 includes a case 520 having an open end 522 and a mouthpiece 524 (FIG. 25) for patient inhalation, a cap 526 secured to and closing the open end 522 of the case 520, and a cover 528 pivotally mounted to the case 520 for covering the mouthpiece 524. As shown in FIG. 22, the inhaler 510 also includes an actuation spring 569, first yoke 566 with opening 572, bellows 540 with crown 574, a reservoir 514, second yoke 568 with hopper 542 and dose counter 516 mounted thereto, and case 520 has transparent window 5130 thereon for viewing dose counter tape indicia 5128. The dose metering system also includes two cams 570 mounted on the mouthpiece cover 528 and movable with the cover 528 between open and closed positions. The cams 570 each include an opening 580 for allowing outwardly extending hinges 582 of the case 520 to pass therethrough and be received in first recesses 584 of the cover 528. The cams 570 also include bosses 586 extending outwardly and received in second recesses 588 of the cover 528, such that the cover 528 pivots about the hinges 582 and the cams 570 move with the cover 528 about the hinges 582. As described in EP-A-1330280, cams 570 act upon cam followers 578 to move second yoke 568 up and down and thereby operate dose counter by engagement of pawl 5138 on the second yoke 568 with teeth 5136. Remaining components of the inhaler are provided as, and operate as described, in EP-A-1330280.

The dose counting system 516 therefore includes a ribbon or tape 5128 (FIGS. 23 & 24), having successive numbers or other suitable indicia printed thereon, in alignment with a transparent window 5130 provided in the housing 18 (see FIG. 22). The dose counting system 516 includes the rotatable stock bobbin 110 (as described above), an indexing spool 5134 rotatable in a single direction, and the ribbon 5128 rolled and received on the bobbin 110 and having a first end 5127 secured to the spool 5134, wherein the ribbon 5128 unrolls from the bobbin 110 so that the indicia are successively displayed as the spool 5134 is rotated or advanced. In FIGS. 23 and 24 the wavelike engagement surface 300 of the bobbin 110 is not shown for the purposes of clarity.

The spool 134 is arranged to rotate upon movement of the yokes 566, 568 to effect delivery of a dose of medicament from reservoir 514, such that the number on the ribbon 5128 is advanced to indicate that another dose has been dispensed by the inhaler 510. The ribbon 5128 can be arranged such that the numbers, or other suitable indicia, increase or

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decrease upon rotation of the spool **5134**. For example, the ribbon **5128** can be arranged such that the numbers, or other suitable indicia, decrease upon rotation of the spool **5134** to indicate the number of doses remaining in the inhaler **510**. Alternatively, the ribbon **5128** can be arranged such that the numbers, or other suitable indicia, increase upon rotation of the spool **5134** to indicate the number of doses dispensed by the inhaler **10**.

The indexing spool **5134** includes radially extending teeth **5136**, which are engaged by pawl **5138** extending from a cam follower **578** of the second yoke **568** upon movement of the yoke to rotate, or advance, the indexing spool **5134**. More particularly, the pawl **5138** is shaped and arranged such that it engages the teeth **5136** and advances the indexing spool **5134** only upon the mouthpiece cover **528** being closed and the yokes **566**, **568** moved back towards the cap **526** of the housing **518**.

The dose counting system **516** also includes a chassis **5140** that secures the dose counting system to the hopper **542** and includes shafts **108**, **5144** for receiving the bobbin **110** and the indexing spool **5134**. As described above with reference to FIGS. 1 to 20, the bobbin shaft **108** is forked and includes radially nubs **5146** for creating a resilient resistance to rotation of the bobbin **110** on the shaft **108** by engaging with the wavelike engagement surface **300** inside the bobbin **110**. A clutch spring **5148** is received on the end of the indexing spool **5134** and locked to the chassis **5140** to allow rotation of the spool **5134** in only a single direction.

Various modifications may be made to the embodiment shown without departing from the scope of the invention as defined by the accompanying claims as interpreted under patent law.

What is claimed is:

1. An inhaler comprising a dose counter and dose counter viewing window, the inhaler being configured to be readied by priming before first use and the dose counter comprising:
 - a tape system having a main elongate tape structure, dosing indicia located on the main elongate tape structure, tape positioning indicia located on the main elongate tape structure, a tape size marker located on the main elongate tape structure indicating a number of dosing indicia on the main elongate tape structure, and priming indicia located on the main elongate tape structure, the priming indicia being located between the dosing indicia and a first end of the main elongate tape structure and visible in the dose counter viewing window before priming before first use, and wherein the first end of the main elongate tape structure is fixed to a tape reel shaft and a second end of the main elongate tape structure is attached to a stock bobbin, and wherein the main elongate tape structure is around both the stock bobbin and tape reel shaft when the priming indicia is visible in the dose counter viewing window before priming before first use.
2. The inhaler of claim 1, wherein the dosing indicia comprise numbers printed on the main elongate tape structure.
3. The inhaler of claim 1, wherein the priming indicia is a priming dot located on the main elongate tape structure that is to be aligned with the viewing window on the inhaler that is visible to a user of the inhaler.
4. The inhaler of claim 1, wherein the tape positioning indicia comprise a series of lines that are each formed across the main elongate tape structure.
5. The inhaler of claim 1, wherein the tape size marker is positioned between said one the first end of the main elongate tape structure and the tape positioning indicia.

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6. The inhaler of claim 1, wherein the tape positioning indicia are positioned between the first end of the main elongate tape structure and the dosing indicia.

7. The inhaler of claim 1, wherein the first end of the main elongate tape structure is fixed to the tape reel shaft.

8. The inhaler of claim 1, wherein the priming indicia is positioned between the dosing indicia and the tape positioning indicia.

9. The inhaler of claim 1, wherein the tape size marker is a pixelated bar code.

10. An inhaler comprising a dose counter and dose counter viewing window, the inhaler being configured to be readied by priming before first use and the dose counter comprising:

- a tape system having a main elongate tape structure, dosing indicia located on the main elongate tape structure, tape positioning indicia located on the main elongate tape structure, and a tape size marker located on the main elongate tape structure indicating a number of dosing indicia on the main elongate tape structure, wherein the tape size marker is positioned between a first end of the main elongate tape structure and the tape positioning indicia,

wherein the first end of the main elongate tape structure is fixed to a tape reel shaft and a second end of the main elongate tape structure is attached to a stock bobbin, and wherein the tape is around both the stock bobbin and tape reel shaft and a portion of the main elongate tape structure between the tape positioning indicia and the dosing indicia is visible in the dose counter viewing window before priming before first use.

11. The inhaler of claim 10, wherein the dosing indicia comprise numbers printed on the main elongate tape structure.

12. The inhaler of claim 10, wherein the tape positioning indicia comprise a series of lines that are each formed across the main elongate tape structure.

13. The inhaler of claim 10, wherein the tape size marker is positioned between the first end of the main elongate tape structure and the dosing indicia.

14. The inhaler of claim 10, wherein the tape size marker is a pixelated bar code.

15. The inhaler of claim 10, wherein said the first of the main elongate tape structure is fixed to the tape reel shaft.

16. The inhaler of claim 10 further comprising priming indicia located on the main elongate tape structure, the priming indicia being located between the dosing indicia and the first end of the main elongate tape structure.

17. The inhaler of claim 16, wherein the tape positioning indicia are positioned between the first end of the tape and the dosing indicia.

18. The inhaler of claim 16, wherein the priming indicia are positioned between the dosing indicia and the tape positioning indicia.

19. The inhaler of claim 16, wherein the priming indicia is a priming dot located on the main elongate tape structure that is to be aligned with the viewing window.

20. An inhaler comprising a dose counter and dose counter viewing window, the inhaler being configured to be readied by priming before first use and the dose counter comprising:

- a tape system having a main elongate tape structure, dosing indicia located on the main elongate tape structure, tape positioning indicia located on the main elongate tape structure so as to be visible in the dose counter viewing window before priming before first use, and priming indicia located on the main elongate tape

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structure, the priming indicia being located between the
tape positioning indicia and the dosing indicia,
wherein a first end of the main elongate tape structure is
attached to a stock bobbin and a second end of the main
elongate tape structure is fixed to a tape reel shaft, and 5
wherein the main elongate tape structure is around both
the stock bobbin and tape reel shaft when the priming
indicia is visible in the dose counter viewing window
before priming before first use.

21. The inhaler of claim 20, wherein the dosing indicia 10
comprise numbers printed on the main elongate tape struc-
ture.

22. The inhaler of claim 20, wherein the priming indicia
is a priming dot located on the main elongate tape structure
that is to be aligned with the viewing window on the inhaler 15
that is visible to a user of the inhaler.

23. The inhaler of claim 20, wherein the tape positioning
indicia comprise a series of lines that are each formed across
the main elongate tape structure.

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EXHIBIT E

(12) **United States Patent**
Walsh et al.

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(54) **DOSE COUNTER FOR INHALER AND
METHOD FOR COUNTING DOSES**

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(Continued)

(58) **Field of Classification Search**
CPC **A61M 11/00**; **A61M 15/00**; **G06M 1/06**
(Continued)

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and Shaft Arrangement."

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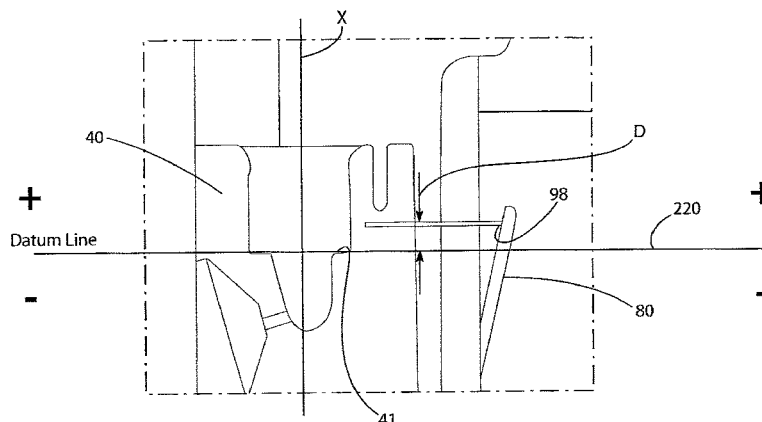
Primary Examiner — Daniel Hess

(74) *Attorney, Agent, or Firm* — Morgan, Lewis &
Bockius, LLP

(57) **ABSTRACT**

A dose counter for a metered dose inhaler includes an
incremental counting system for counting doses. The incre-
mental counting system has a main body, an actuator
arranged to be driven in response to canister motion and to
drive an incremental output member in response to canister
motion. The actuator and incremental output member are
configured to have predetermined canister fire and count
configurations in a canister fire sequence. The canister fire
configuration is determined by a position of the actuator
relative to a datum at which the canister fires medicament

(Continued)



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and the count configuration is determined by a position of the actuator relative to the datum at which the incremental count system makes an incremental count. The actuator is arranged to reach a position in the count configuration at or after a position in the canister fire configuration.

13 Claims, 17 Drawing Sheets

Related U.S. Application Data

- 13/110,532, filed on May 18, 2011, now Pat. No. 8,978,966.
- (60) Provisional application No. 61/345,763, filed on May 18, 2010, provisional application No. 61/417,659, filed on Nov. 29, 2010.
- (51) **Int. Cl.**
A61M 15/00 (2006.01)
G06M 1/24 (2006.01)
- (52) **U.S. Cl.**
CPC *A61M 15/0025* (2014.02); *A61M 15/0026* (2014.02); *A61M 15/0065* (2013.01); *A61M 15/0071* (2014.02); *G06M 1/246* (2013.01); *A61M 2202/064* (2013.01); *A61M 2205/6063* (2013.01); *A61M 2207/00* (2013.01); *A61M 2207/10* (2013.01); *Y10T 29/49* (2015.01); *Y10T 29/49764* (2015.01); *Y10T 29/49826* (2015.01)
- (58) **Field of Classification Search**
USPC 235/103; 128/200.23
See application file for complete search history.

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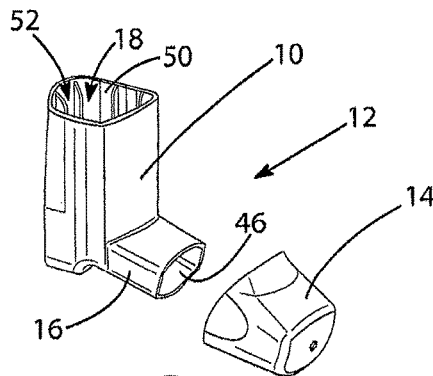


FIG. 1

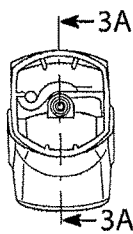


FIG. 2

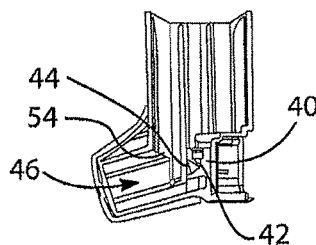


FIG. 3A

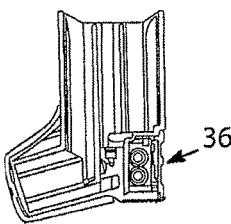


FIG. 3B

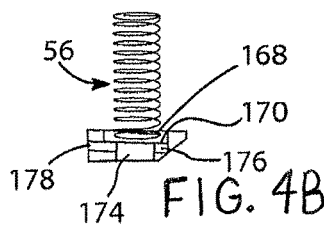


FIG. 4B

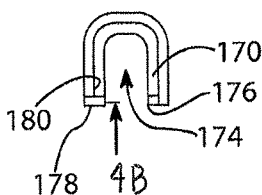


FIG. 4C

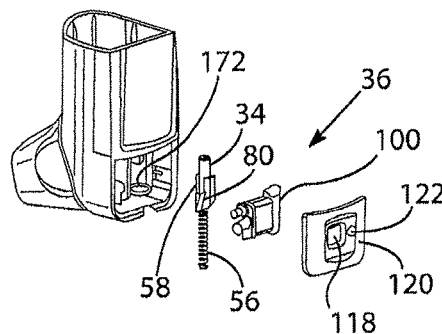


FIG. 4A

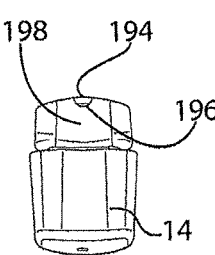


FIG. 5

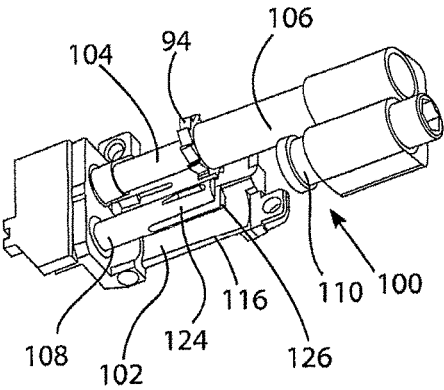


FIG. 6A

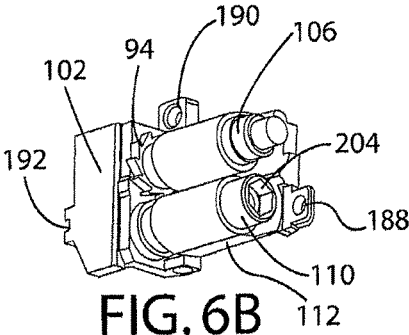


FIG. 6B

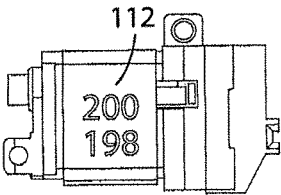


FIG. 6C

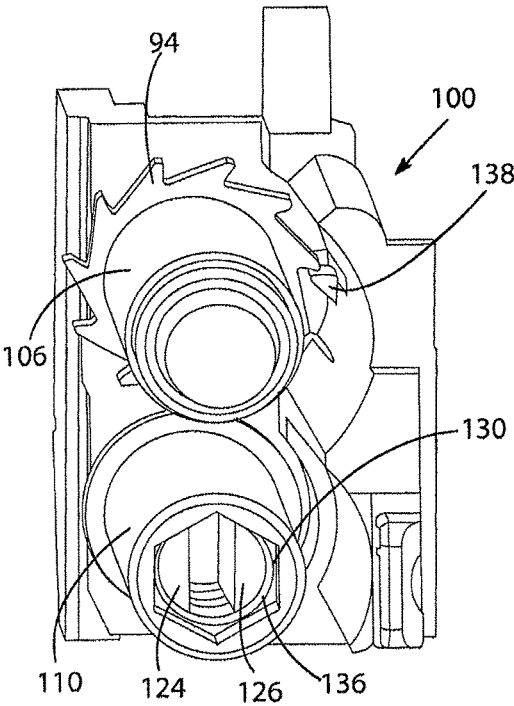


FIG. 6D

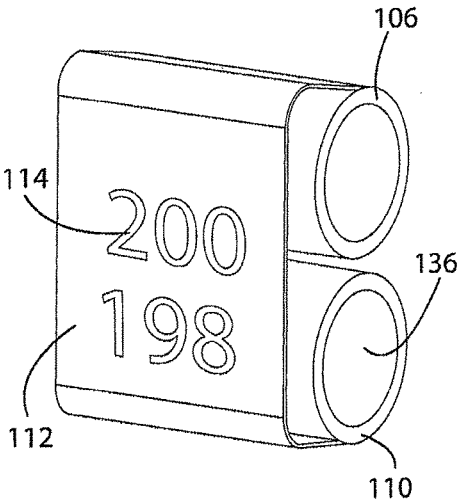


FIG. 6E

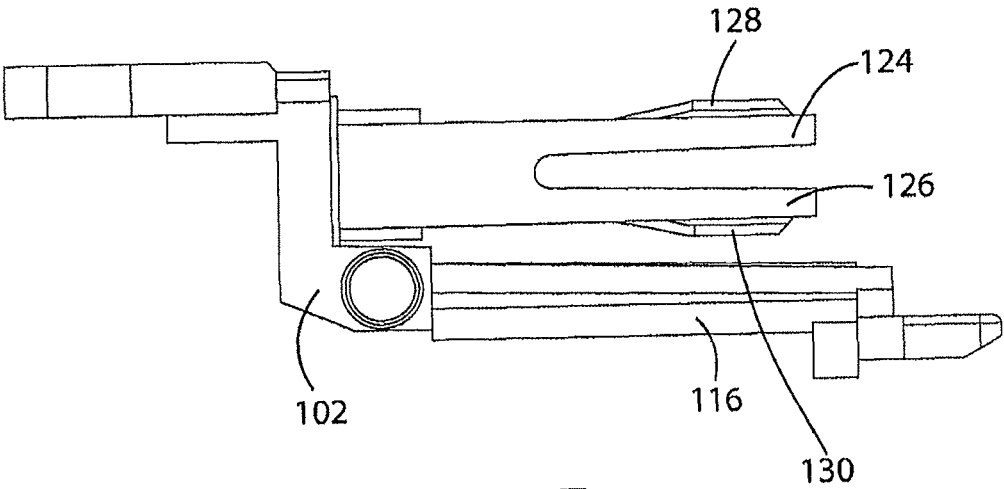


FIG. 6F

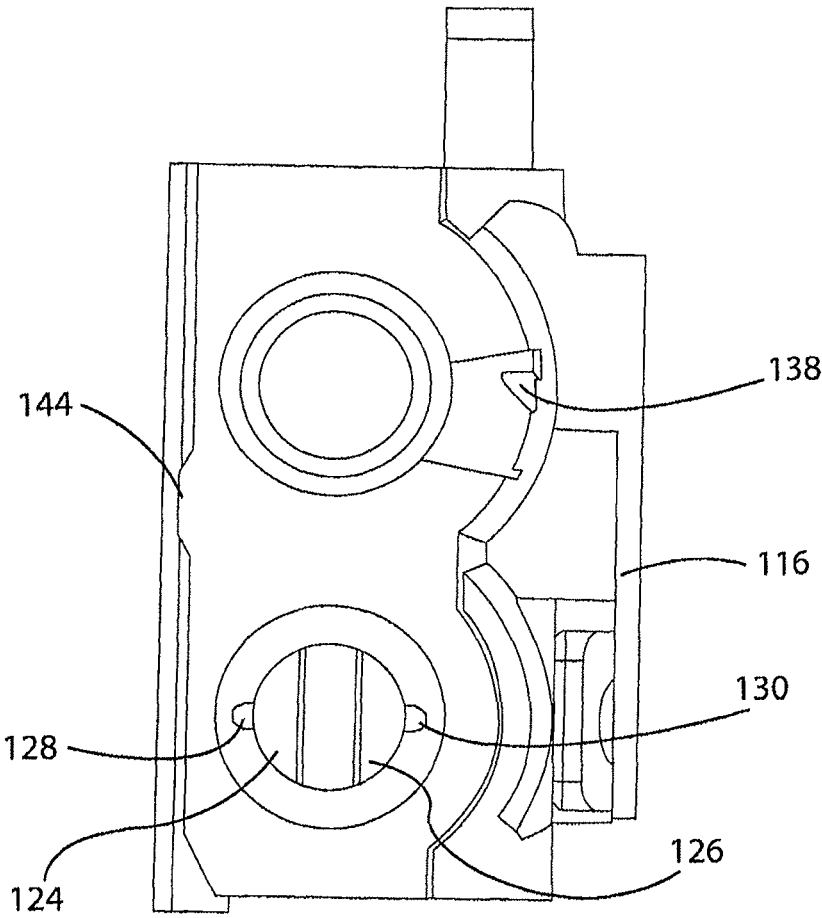


FIG. 6G

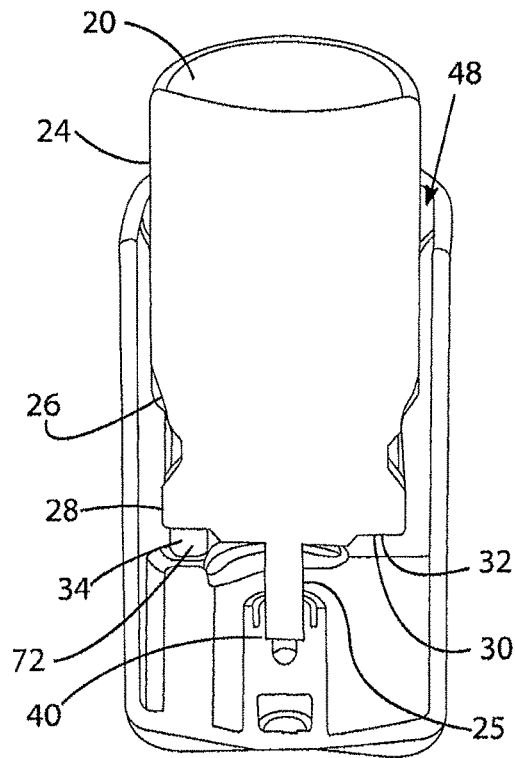


FIG. 7A

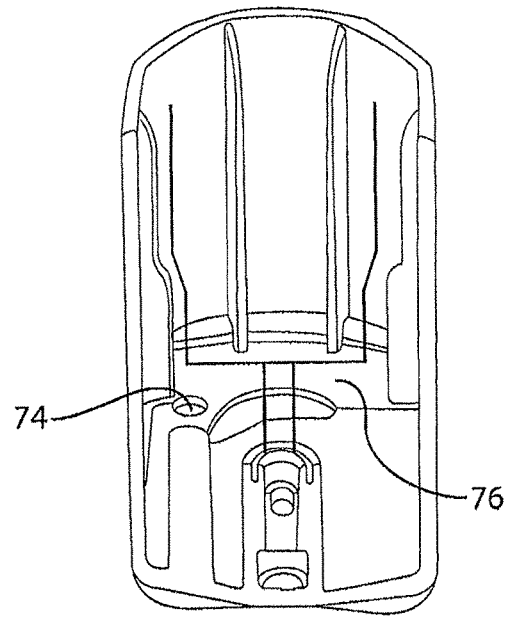


FIG. 7B

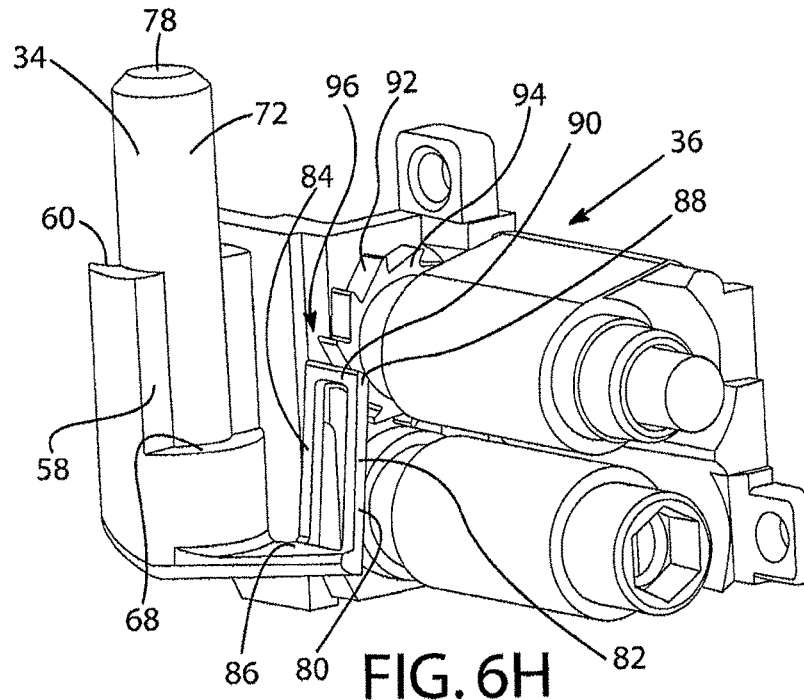


FIG. 6H

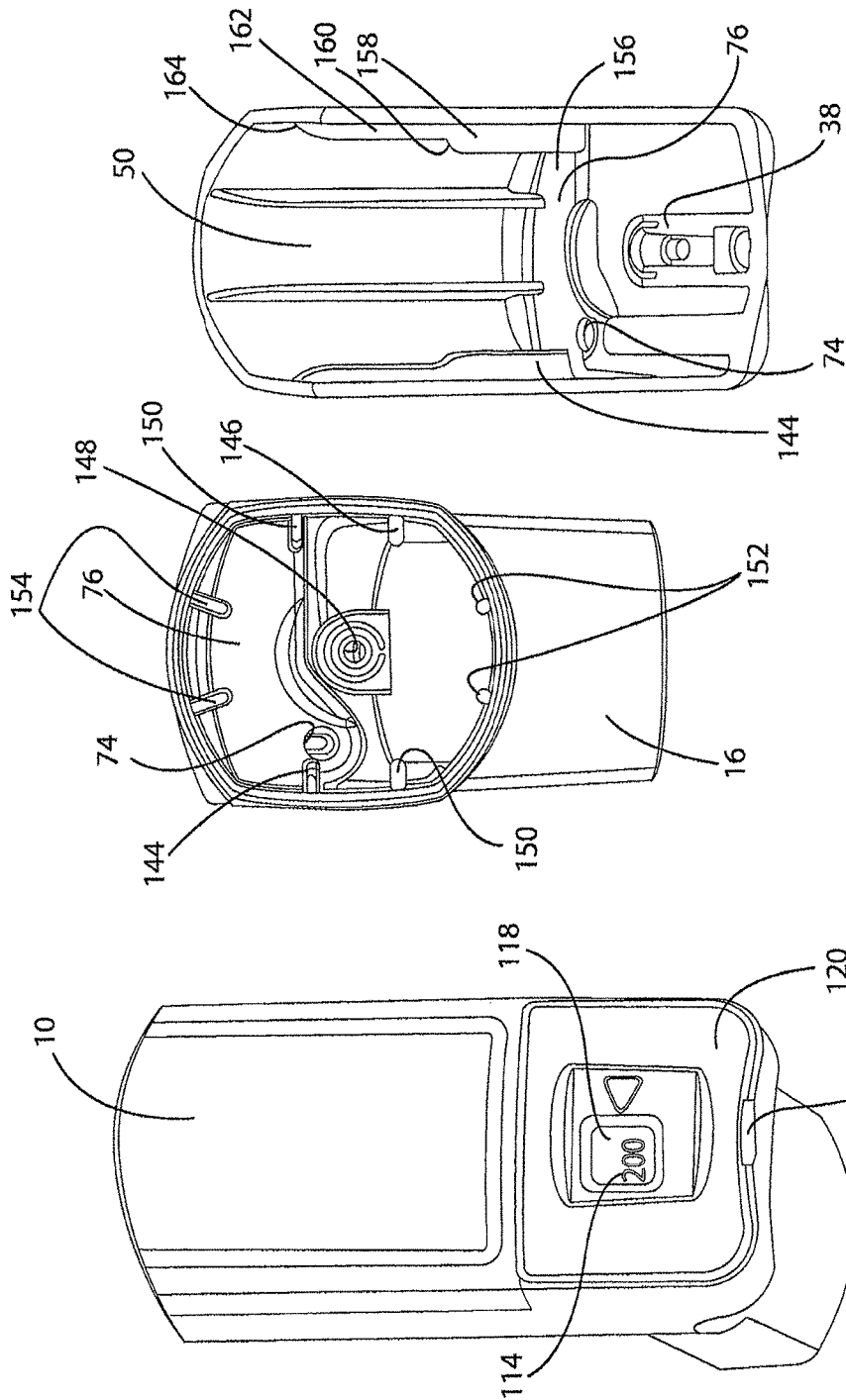


FIG. 7C

FIG. 7D

FIG. 8D

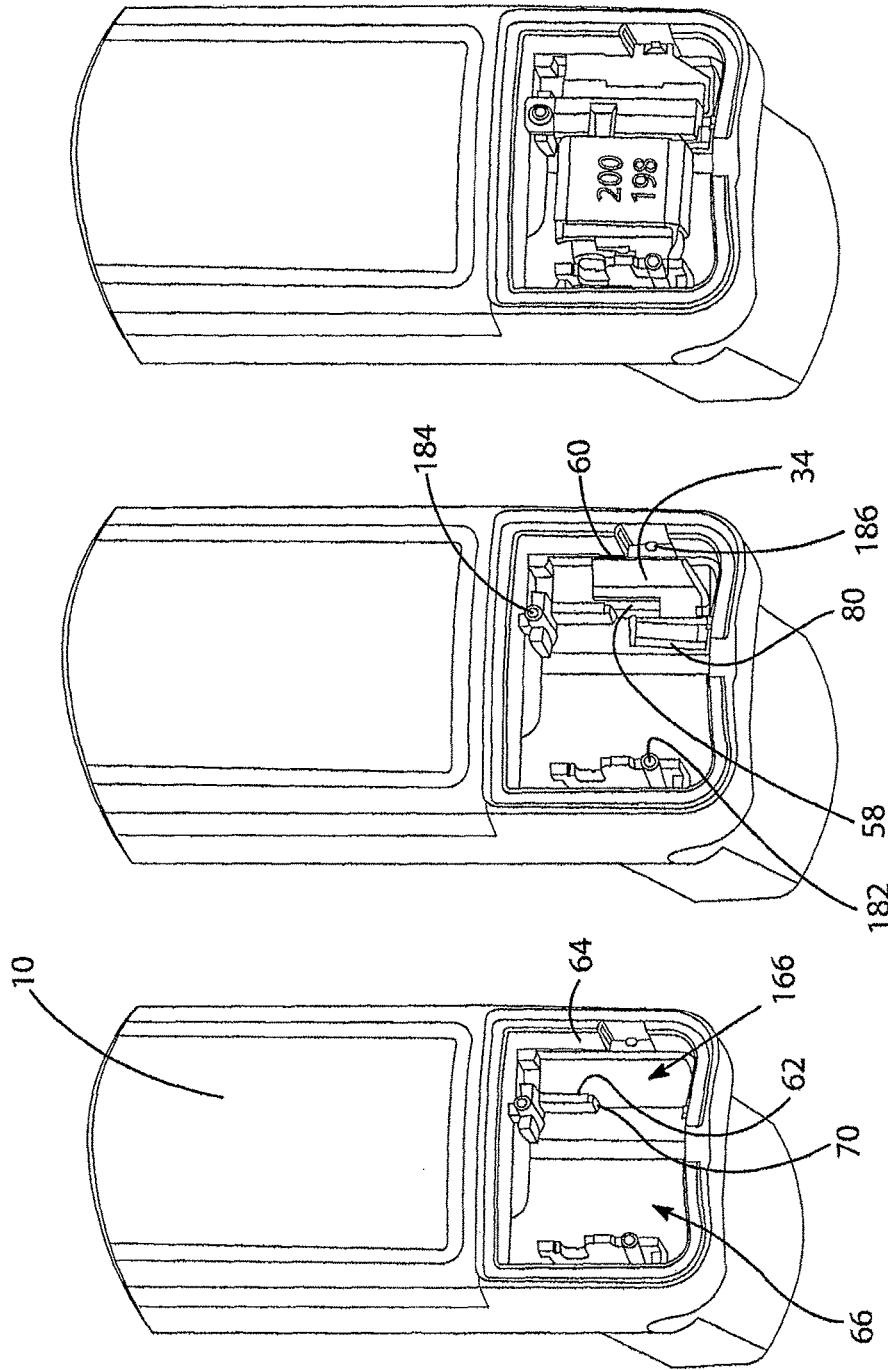


FIG. 8C

FIG. 8B

FIG. 8A

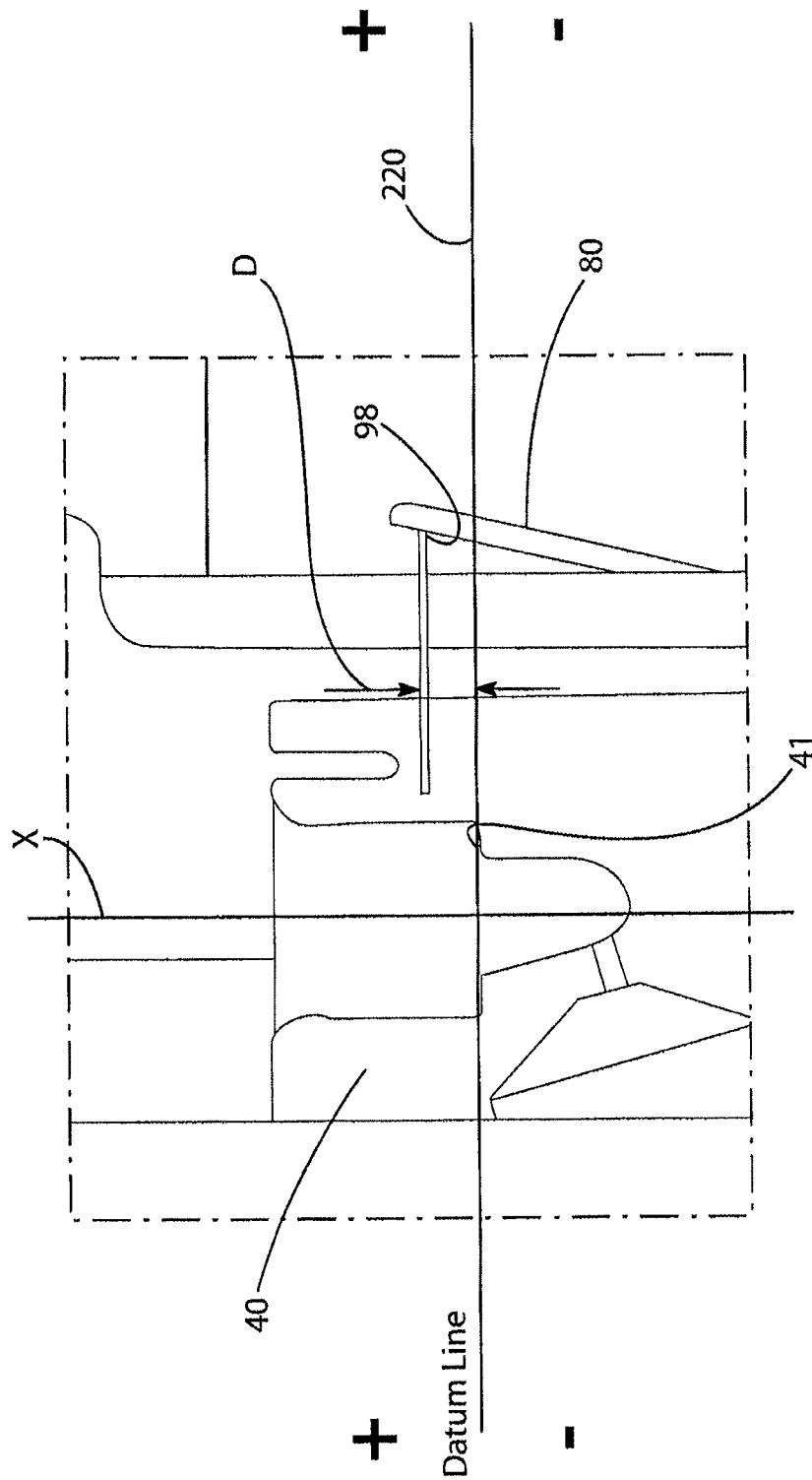


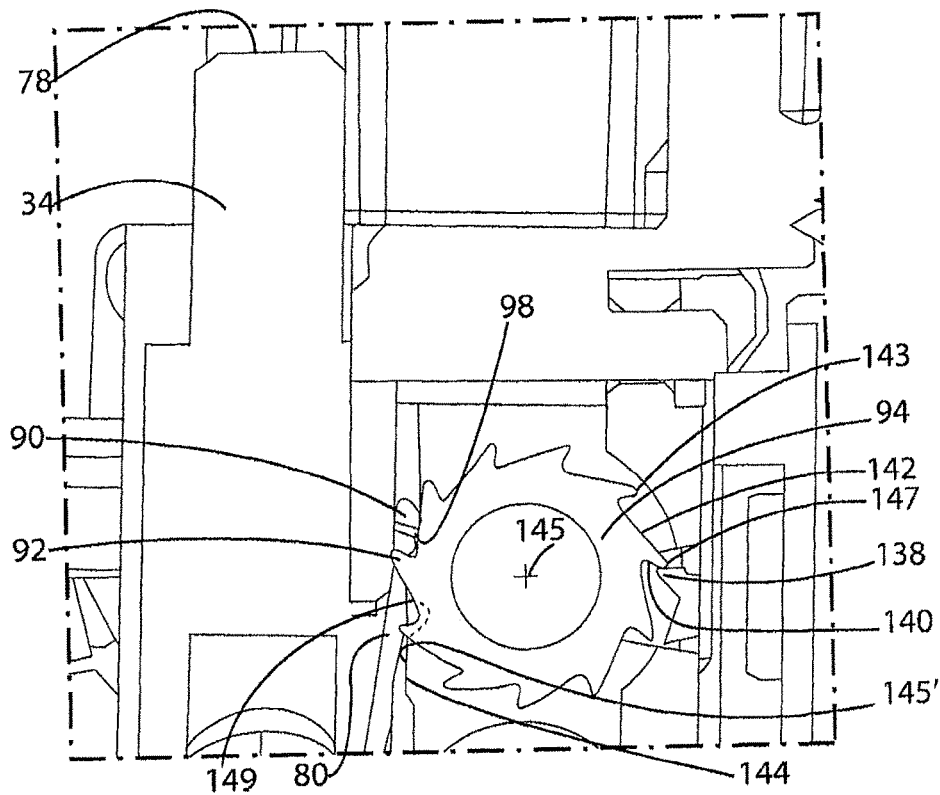
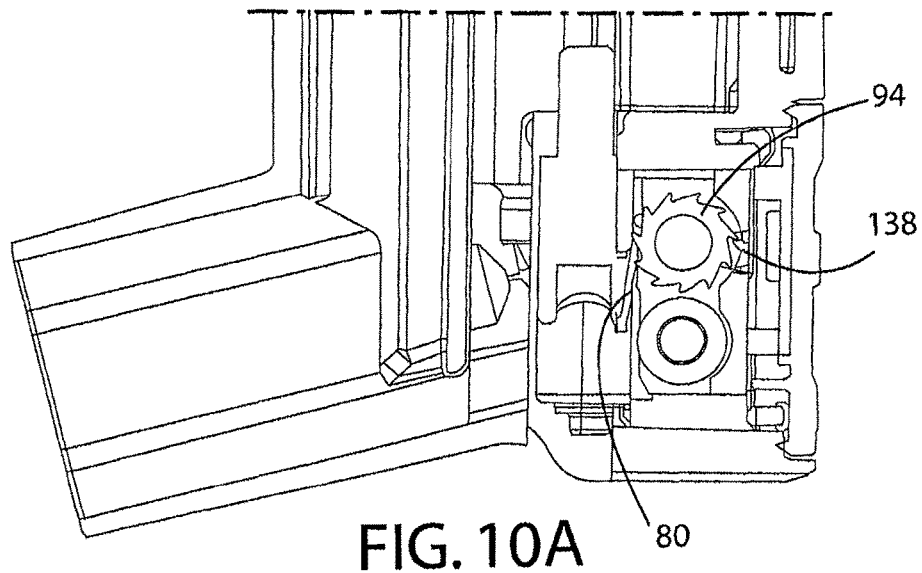
FIG. 9

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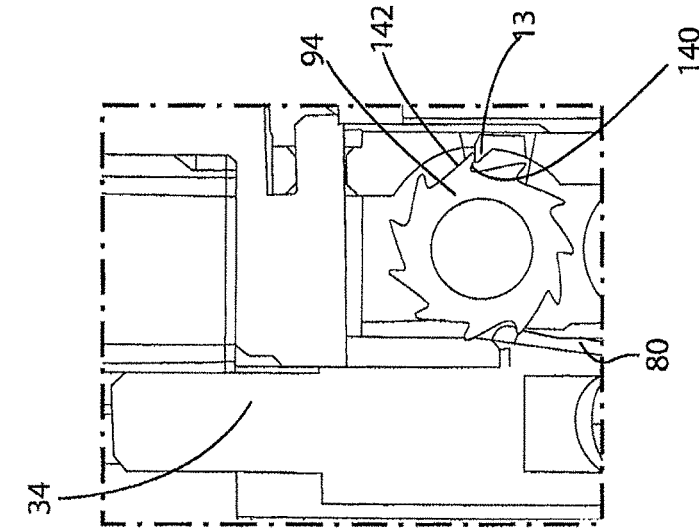


FIG. 10E

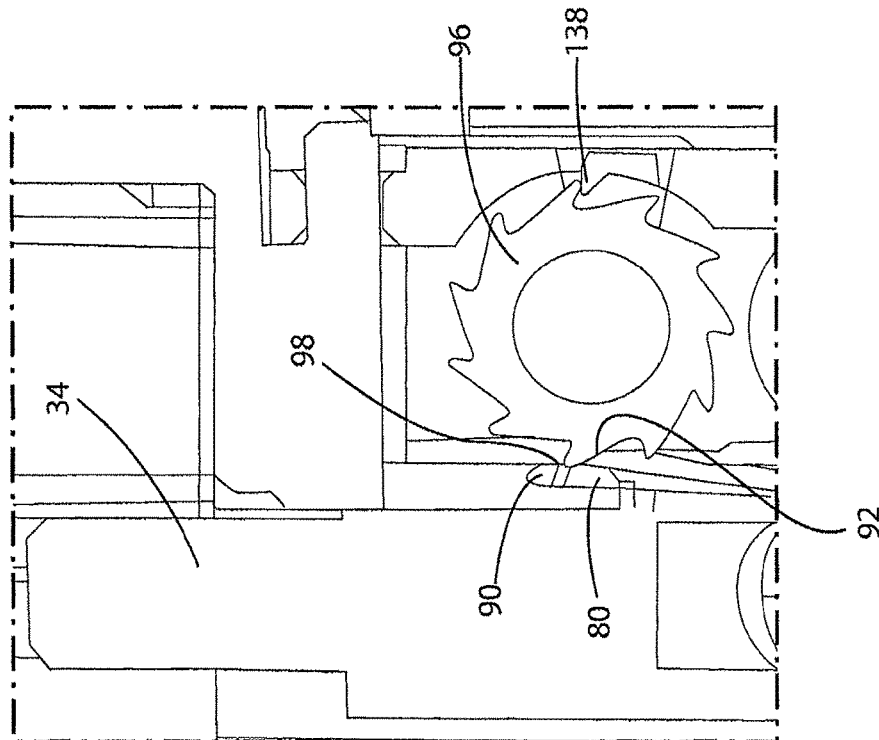


FIG. 10C

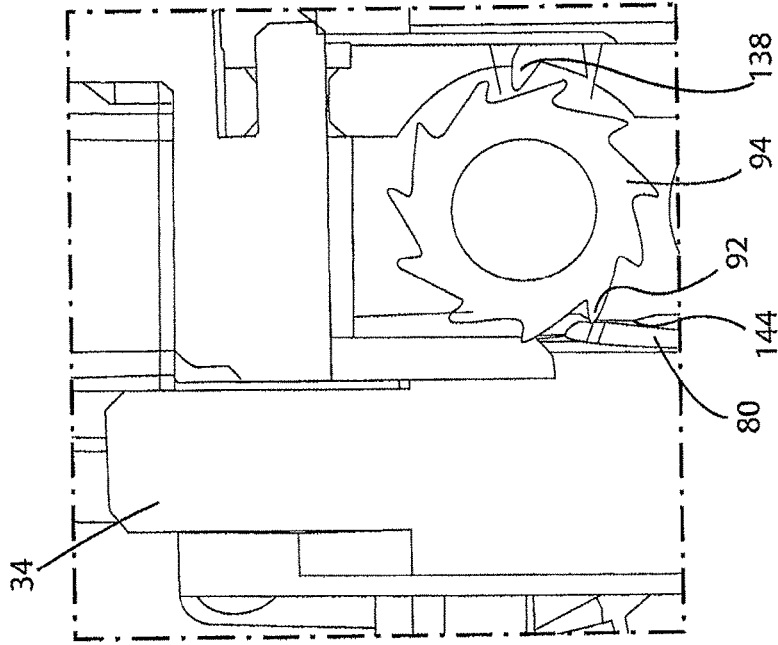


FIG. 10F

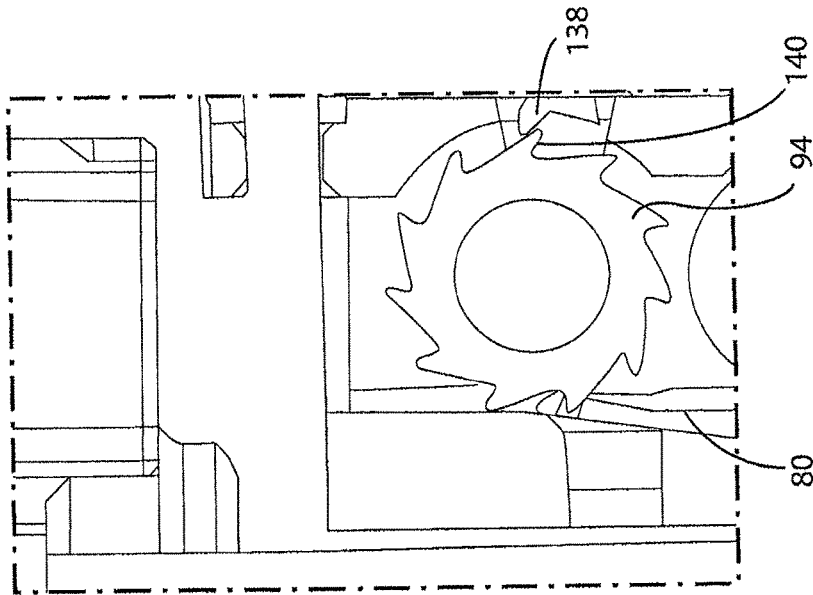


FIG. 10D

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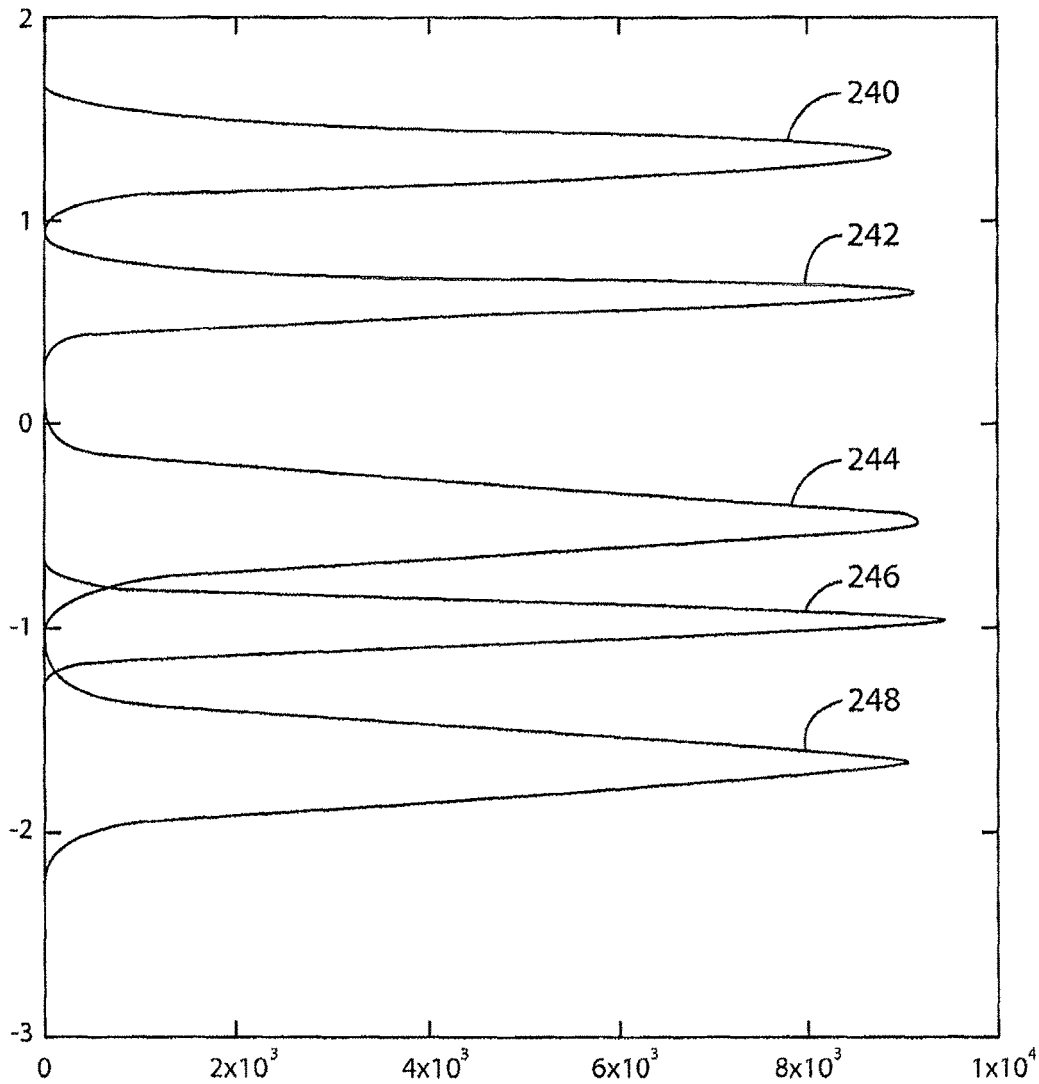


FIG. 11

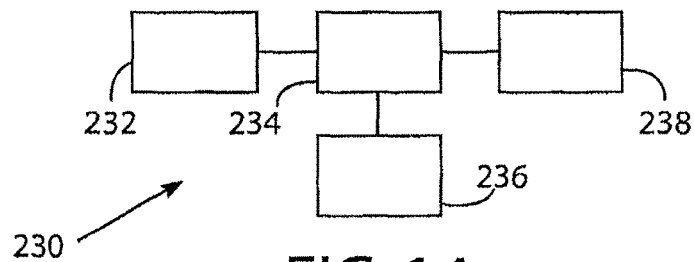


FIG. 14

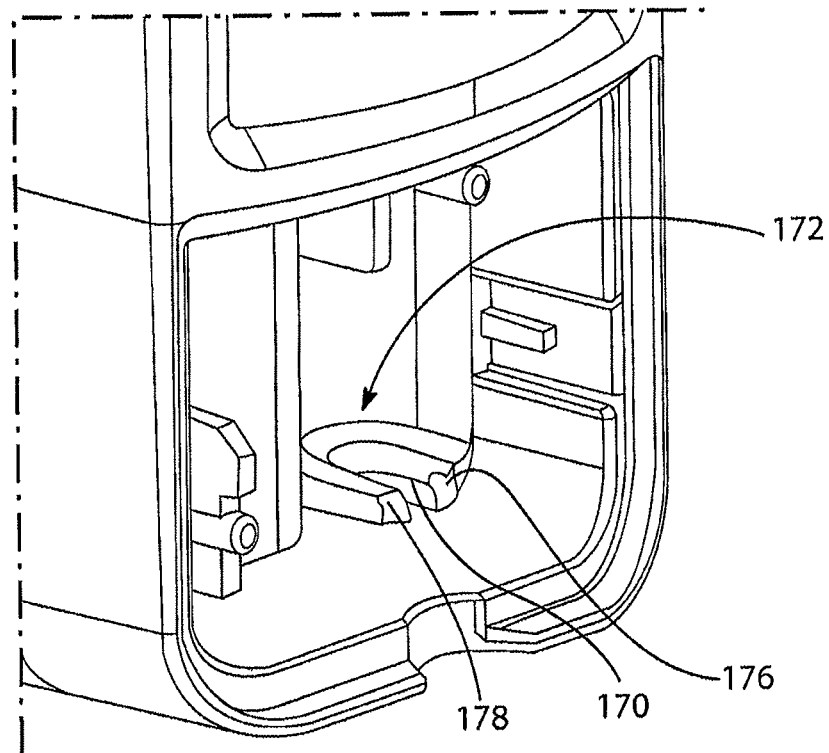


FIG. 12

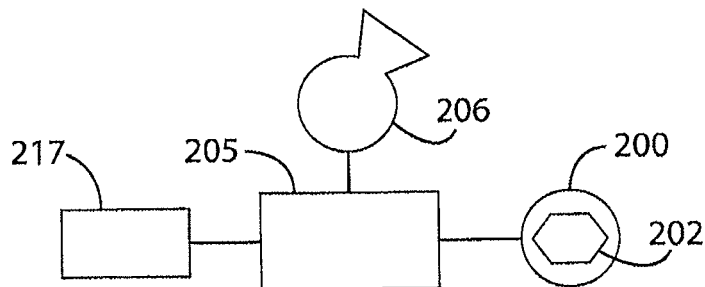
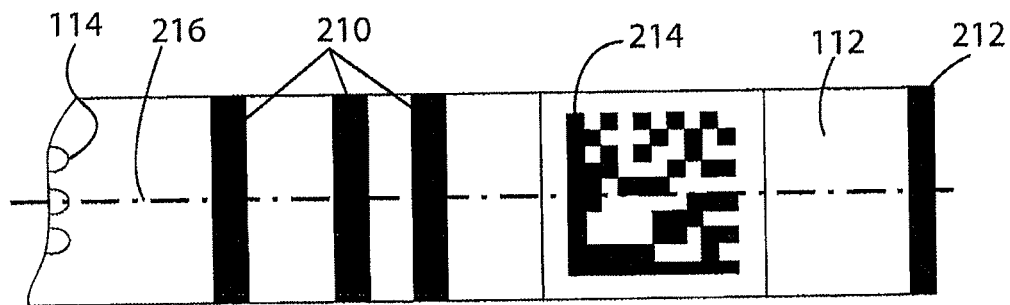


FIG. 13

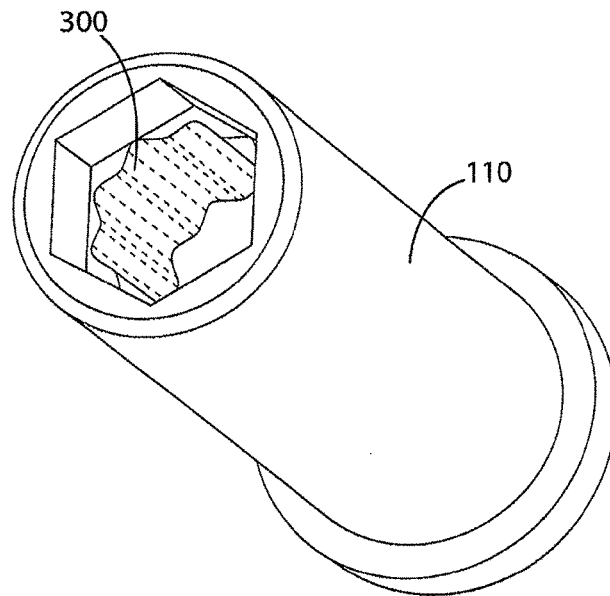


FIG. 15

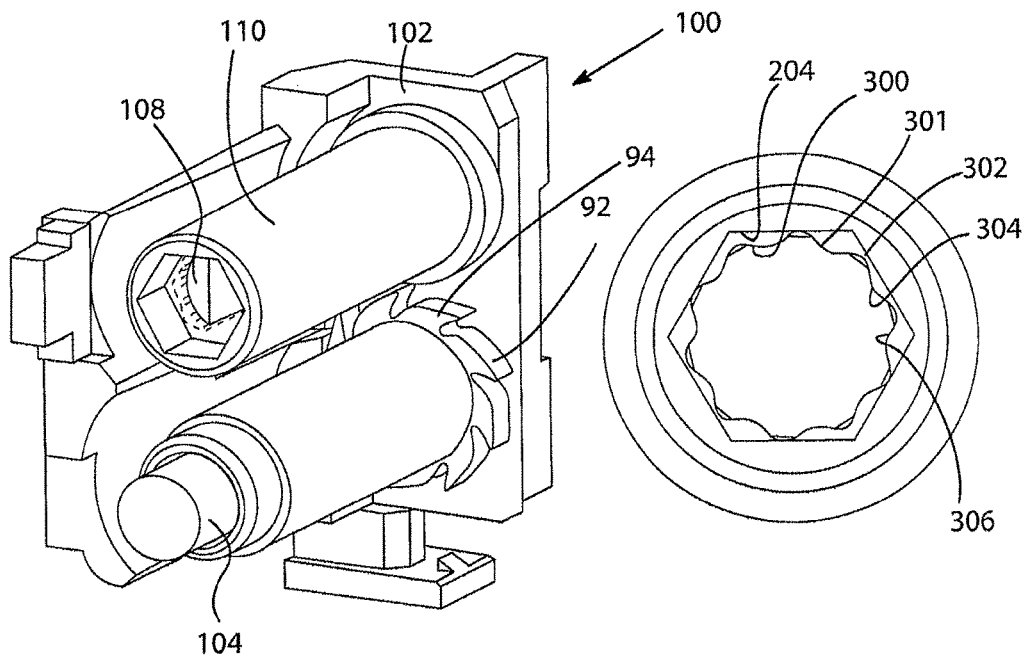


FIG. 20

FIG. 16

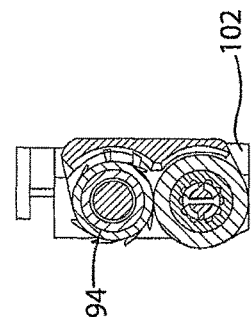


FIG. 19A

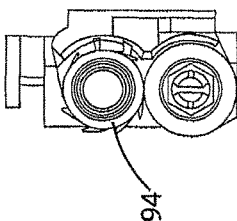


FIG. 19B

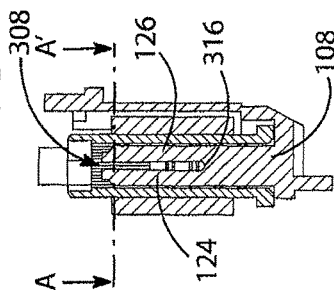


FIG. 19C

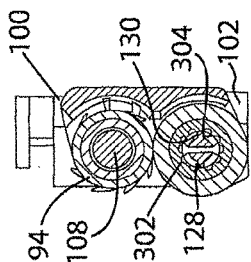


FIG. 18A

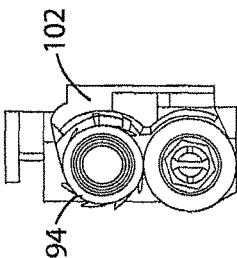


FIG. 18B

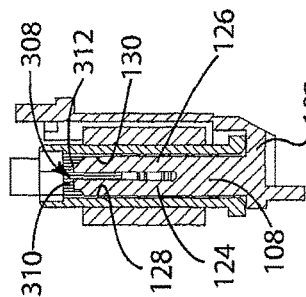


FIG. 18C

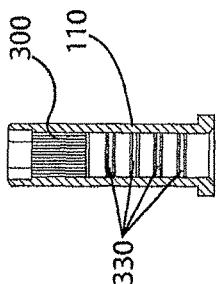


FIG. 17

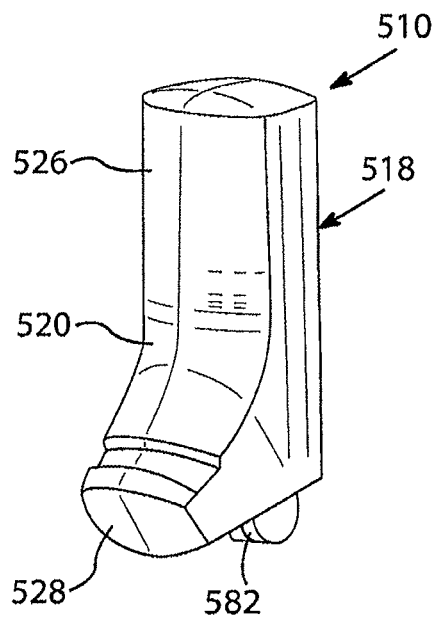


FIG. 21

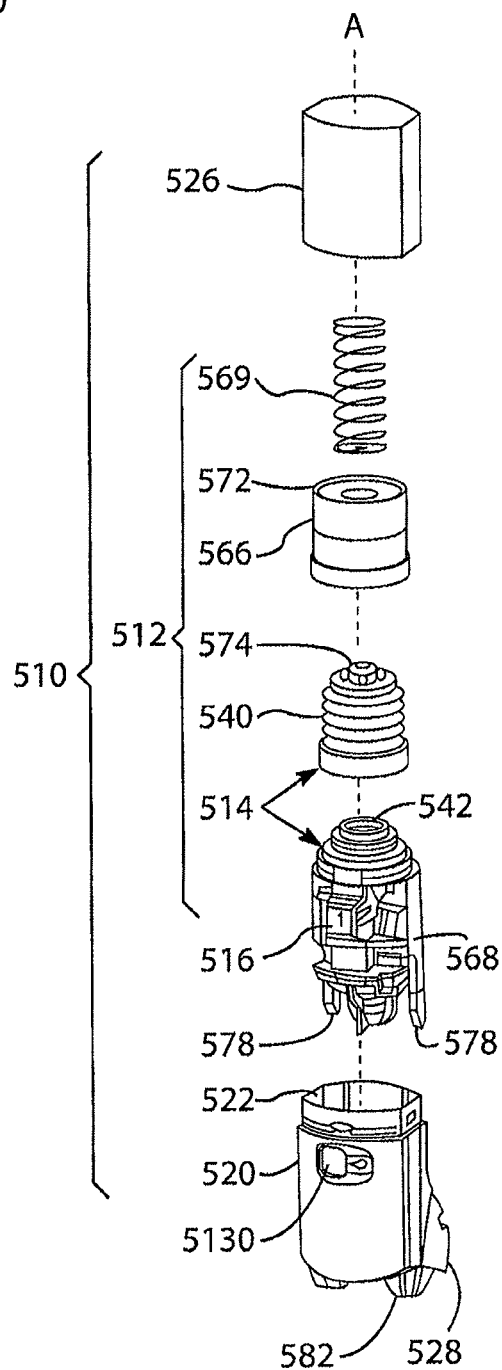


FIG. 22

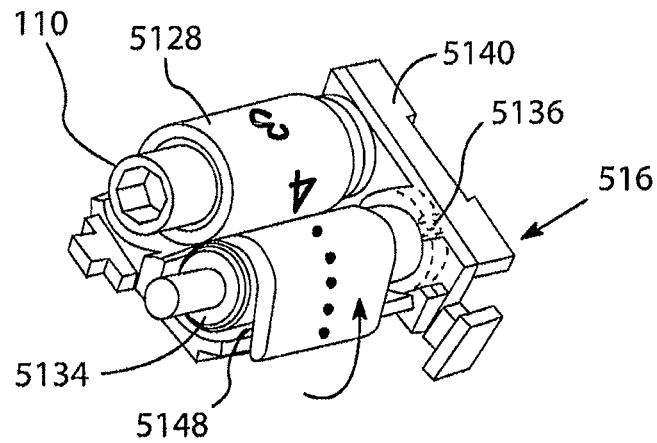


FIG. 23

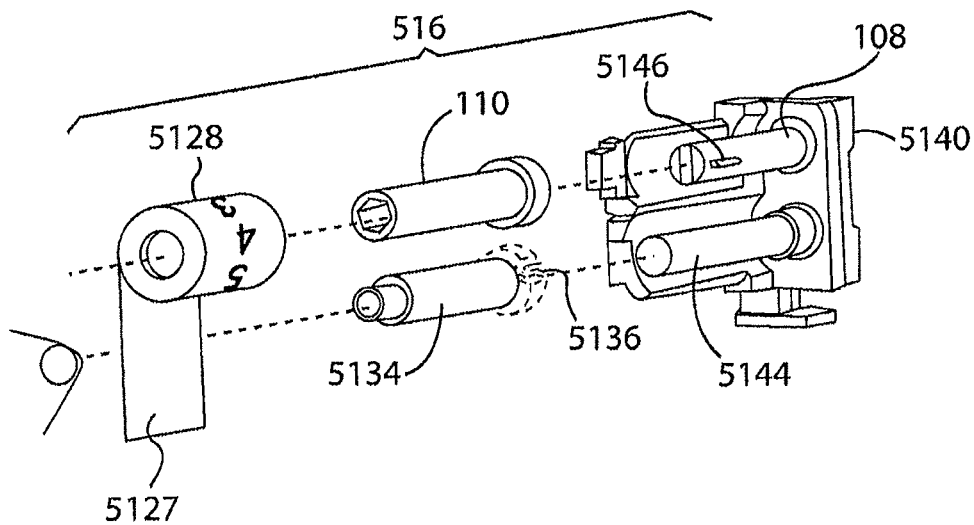


FIG. 24

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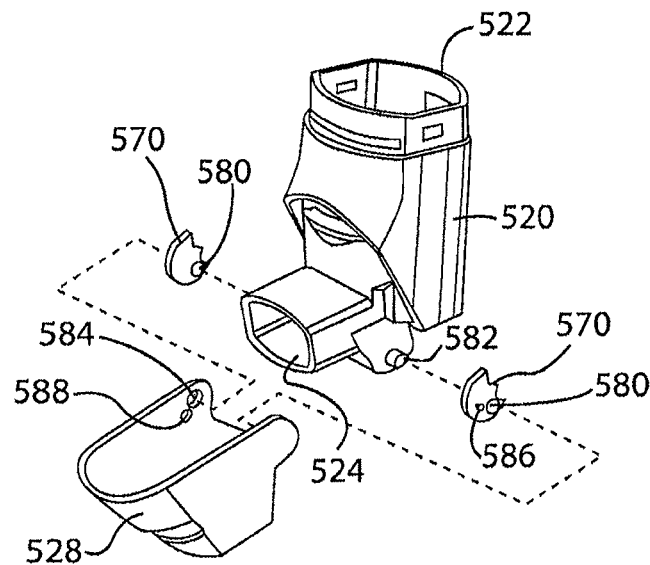


FIG. 25

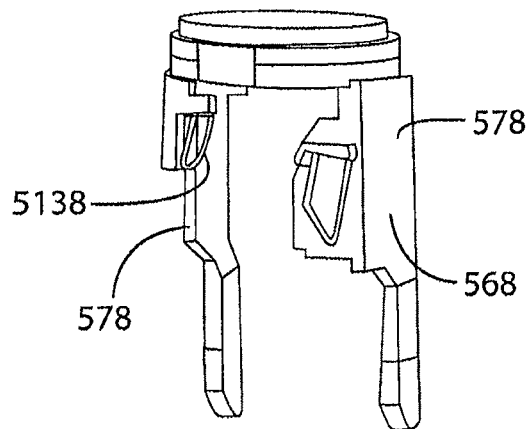


FIG. 26

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1

DOSE COUNTER FOR INHALER AND METHOD FOR COUNTING DOSES

CROSS-REFERENCE TO RELATED APPLICATIONS

This patent application is a continuation patent application of U.S. Non-Provisional Patent Application No. 14/103,353, filed Dec. 11, 2013, which is a divisional patent application of U.S. Non-Provisional Patent Application No. 13/110,532, filed May 18, 2011, which claims priority to U.S. Provisional Patent Application No. 61/345,763, filed May 18, 2010, and U.S. Provisional Patent Application No. 61/417,659, filed Nov. 29, 2010, each of which is incorporated herein by reference in its entirety for all purposes.

FIELD OF THE INVENTION

The present invention relates to dose counters for inhalers, inhalers and methods of assembly thereof. The invention is particularly applicable to metered dose inhalers including dry power medicament inhalers, breath actuated inhalers and manually operated metered dose medicament inhalers.

BACKGROUND OF THE INVENTION

Metered dose inhalers can comprise a medicament-containing pressurised canister containing a mixture of active drug and propellant. Such canisters are usually formed from a deep-drawn aluminium cup having a crimped lid which carries a metering valve assembly. The metering valve assembly is provided with a protruding valve stem which, in use is inserted as a push fit into a stem block in an actuator body of an inhaler having a drug delivery outlet. In order to actuate a manually operable inhaler, the user applies by hand a compressive force to a closed end of the canister and the internal components of the metering valve assembly are spring loaded so that a compressive force of approximately 15 to 30N is required to activate the device in some typical circumstances.

In response to this compressive force the canister moves axially with respect to the valve stem and the axial movement is sufficient to actuate the metering valve and cause a metered quantity of the drug and the propellant to be expelled through the valve stem. This is then released into a mouthpiece of the inhaler via a nozzle in the stem block, such that a user inhaling through the outlet of the inhaler will receive a dose of the drug.

A drawback of self-administration from an inhaler is that it is difficult to determine how much active drug and/or propellant are left in the inhaler, if any, especially of the active drug and this is potentially hazardous for the user since dosing becomes unreliable and backup devices not always available.

Inhalers incorporating dose counters have therefore become known.

WO 98/028033 discloses an inhaler having a ratchet mechanism for driving a tape drive dose counter. A shaft onto which tape is wound has a friction clutch or spring for restraining the shaft against reverse rotation.

EP-A-1486227 discloses an inhaler for dry powered medicament having a ratchet mechanism for a tape dose counter which is operated when a mouthpiece of the inhaler is closed. Due to the way in which the mouthpiece is opened and closed, and actuation pawl of the device which is mounted on a yoke, travels a known long stroke of consistent length as the mouthpiece is opened and closed.

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WO 2008/119552 discloses a metered-dose inhaler which is suitable for breath-operated applications and operates with a known and constant canister stroke length of 3.04 mm \pm 0.255 mm. A stock bobbin of the counter, from which a tape is unwound, rotates on a shaft having a split pin intended to hold the stock bobbin taut. However, some dose counters do not keep a particularly reliable count, such as if they are dropped onto a hard surface.

More recently, it has become desirable to improve dose counters further and, in particular, it is felt that it would be useful to provide extremely accurate dose counters for manually-operated canister-type metered dose inhalers. Unfortunately, in these inhalers, it has been found in the course of making the present invention that the stroke length of the canister is to a very large extent controlled on each dose operation by the user, and by hand. Therefore, the stroke length is highly variable and it is found to be extremely difficult to provide a highly reliable dose counter for these applications. The dose counter must not count a dose when the canister has not fired since this might wrongly indicate to the user that a dose has been applied and if done repeatedly the user would throw away the canister or whole device before it is really time to change the device due to the active drug and propellant reaching a set minimum. Additionally, the canister must not fire without the dose counter counting because the user may then apply another dose thinking that the canister has not fired, and if this is done repeatedly the active drug and/or propellant may run out while the user thinks the device is still suitable for use according to the counter. It has also been found to be fairly difficult to assembly some known inhaler devices and the dose counters therefor. Additionally, it is felt desirable to improve upon inhalers by making them easily usable after they have been washed with water.

The present invention aims to alleviate at least to a certain extent one or more of the problems of the prior art.

SUMMARY OF THE INVENTION

According to a first aspect of the present invention there is provided a dose counter for an inhaler, the dose counter having a counter display arranged to indicate dosage information, a drive system arranged to move the counter display incrementally in a first direction from a first station to a second station in response to actuation input, wherein a regulator is provided which is arranged to act upon the counter display at the first station to regulate motion of the counter display at the first station to incremental movements.

The regulator is advantageous in that it helps prevent unwanted motion of the counter display if the counter is dropped.

According to a further aspect of the present invention, the regulator provides a resistance force of greater than 0.1 N against movement of the counter display. According to still a further aspect of the present invention, the resistance force is greater than 0.3 N. According to yet a further aspect of the present invention, the resistance force is from 0.3 to 0.4 N.

Preferably, the counter comprises a tape.

Preferably, the tape has dose counter indicia displayed thereon. The first station may comprise a region of the dose counter where tape is held which is located before a display location, such as a display window, for the counter indicia.

The first station may comprise a first shaft, the tape being arranged on the first shaft and to unwind therefrom upon movement of the counter display.

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The first shaft may be mounted for rotation relative to a substantially rotationally fixed element of the dose counter.

The regulator may comprise at least one projection which is arranged on one of the first shaft and the substantially rotationally fixed element and to engage incrementally with one or more formations on the other of the first shaft and the substantially rotationally fixed element.

At least two said projections may be provided. Exactly two said projections may be provided.

Each projection may comprise a radiused surface.

The at least one projection may be located on the substantially fixed element which may comprise a fixed shaft which is fixed to a main body of the dose counter, the first shaft being rotationally mounted to the fixed shaft.

Preferably, the fixed shaft has at least two resiliently flexible legs (or forks). Each leg may have at least one said projection formed in an outwardly facing direction thereon, said one or more formations being formed on an inwardly facing engagement surface of the first shaft, said at least one projection being arranged to resiliently engage said one or more formations. Preferably, a series of said formations are provided. An even number of said formations may be provided. Eight to twelve of said formations may be provided. In one embodiment, ten said formations are provided.

Each said formation may comprise a concavity formed on an engagement surface. Each concavity may comprise a radiused surface wall portion which preferably merges on at least one side thereof into a flat wall portion surface. The engagement surface may include a series of said concavities, and convex wall portions of the engagement surface may be formed between each adjacent two said concavities, each said convex wall portion comprising a convex radiused wall portion.

Each convex radiused wall portion of each convex wall portion may be connected by said flat wall portion surfaces to each adjacent concavity.

The fixed shaft may comprise a split pin with fork legs and each projection may be located on a said fork leg.

The first shaft may comprise a substantially hollow bobbin.

Said at least one formation may be located on an inner surface of the bobbin. In other embodiments it may be located on an outer surface thereof. Said engagement surface may extend partially along said bobbin, a remainder of the respective inner or outer surface having a generally smooth journal portion along at least a portion thereof.

The drive system may comprise a tooth ratchet wheel arranged to act upon a second shaft which is located at the second station, the second shaft being rotatable to wind the tape onto the second shaft.

The second shaft may be located on a main body of the dose counter spaced from and parallel to the first shaft.

The ratchet wheel may be fixed to the second shaft is arranged to rotate therewith. The ratchet wheel may be secured to an end of the second shaft and aligned coaxially with the second shaft.

The dose counter may include anti-back drive system which is arranged to restrict motion of the second shaft. The anti-back drive system may include a substantially fixed tooth arranged to act upon teeth of the ratchet wheel.

According to a further aspect of the present invention, a dose counter includes an anti-back drive system which is arranged to restrict motion of the second shaft in a tape winding direction.

According to a further aspect of the present invention there is provided a shaft for holding counter tape in a dose counter for an inhaler, the shaft having an engagement

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surface including incrementally spaced formations located around a periphery thereof, the formations comprising a series of curved concavities and convex portions.

The shaft may comprise a hollow bobbin.

The engagement surface may be a generally cylindrical inwardly directed surface.

The engagement surface may include a flat surface wall portion joining each concavity and convex wall portion.

Each concavity may comprise a radiused wall portion.

Each convex wall portion may comprise a radiused wall portion.

Said concavities may be regularly spaced around a longitudinal axis of the shaft.

Said convex wall portions may be regularly spaced around a longitudinal axis of the shaft.

In some embodiments there may be from eight to twelve said concavities and/or convex wall portions regularly spaced around a longitudinal axis thereof.

One embodiment includes ten said concavities and/or convex wall portions regularly spaced around a longitudinal axis of the shaft.

According to a further aspect of the present invention there is provided a shaft and counter tape assembly for use in a dose counter for an inhaler, the assembly comprising a rotatable shaft and a counter tape which is wound around the shaft and is adapted to unwind therefrom upon inhaler actuation, the shaft having an engagement surface which includes incrementally spaced formations located around a periphery thereof.

According to a further aspect of the present invention there is provided an inhaler for the inhalation of medication and the like, the inhaler including a dose counter as in the first aspect of the present invention.

A preferred construction consists of a manually operated metered dose inhaler including a dose counter chamber including a dose display tape driven by a ratchet wheel which is driven in turn by an actuator pawl actuated by movement of a canister, the tape unwinding from a stock bobbin during use of the inhaler, a rotation regulator being provided for the stock bobbin and comprising a wavelike engagement surface with concavities which engage against control elements in the form of protrusions on resilient forks of a split pin thereby permitting incremental unwinding of the stock bobbin yet resisting excessive rotation if the inhaler is dropped onto a hard surface.

According to another aspect of the present invention there is provided a dose counter for a metered dose inhaler having a body arranged to retain a medicament canister of predetermined configuration for movement of the canister relative thereto; the dose counter comprising: an incremental counting system for counting doses, the incremental counting system having a main body, an actuator arranged to be driven in response to canister motion and to drive an incremental output member in response to canister motion, the actuator and incremental output member being configured to have predetermined canister fire and count configurations in a canister fire sequence, the canister fire configuration being determined by a position of the actuator relative to a datum at which the canister fires medicament and the count configuration being determined by a position of the actuator relative to the datum at which the incremental count system makes an incremental count, wherein the actuator is arranged to reach a position thereof in the count configuration at or after a position thereof in the canister fire configuration.

This arrangement has been found to be highly advantageous since it provides an extremely accurate dose counter

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which is suitable for use with manually operated metered dose inhalers. It has been found that dose counters with these features have a failure rate of less than 50 failed counts per million full canister activation depressions. It has been found in the course of making the present invention that highly reliable counting can be achieved with the dose counter counting at or soon after the point at which the canister fires. It has been is covered by the present inventors that momentum and motion involved in firing the canister, and in some embodiments a slight reduction in canister back pressure on the user at the time of canister firing, can very reliably result in additional further motion past the count point.

The actuator and incremental counting system may be arranged such that the actuator is displaced less than 1 mm, typically 0.25 to 0.75 mm, more preferably about 0.4 to 0.6 mm, relative to the body between its location in the count and fire configurations, about 0.48 mm being preferred. The canister, which can move substantially in line with the actuator, can reliably move this additional distance so as to achieve very reliable counting.

The incremental count system may comprise a ratchet mechanism and the incremental output member may comprise a ratchet wheel having a plurality of circumferentially spaced teeth arranged to engage the actuator.

The actuator may comprise an actuator pawl arranged to engage on teeth of the ratchet wheel. The actuator pawl may be arranged to be connected to or integral with an actuator pin arranged to engage and be depressed by a medicament canister bottom flange. The actuator pawl may be generally U-shaped having two parallel arms arranged to pull on a central pawl member arranged substantially perpendicular thereto. This provides a very reliable actuator pawl which can reliably pull on the teeth of the ratchet wheel.

The incremental count system may include a tape counter having tape with incremental dose indicia located thereon, the tape being positioned on a tape stock bobbin and being arranged to unwind therefrom.

The actuator and incremental output member may be arranged to provide a start configuration at which the actuator is spaced from the ratchet output member, a reset configuration at which the actuator is brought into engagement with the incremental output member during a canister fire sequence, and an end configuration at which the actuator disengages from the ratchet output during a canister fire sequence.

The actuator may be arranged to be located about 1.5 to 2.0 mm, from its location in the fire configuration, when in the start configuration, about 1.80 mm being preferred.

The actuator may be arranged to be located about 1.0 to 1.2 mm, from its location in the fire configuration, when in the reset configuration, about 1.11 mm being preferred.

The actuator may be arranged to be located about 1.1 to 1.3 mm, from its location in the fire configuration, when in the end configuration, about 1.18 mm being preferred.

These arrangements provide extremely reliable dose counting, especially with manually operated canister type metered dose inhalers.

The main body may include a formation for forcing the actuator to disengage from the incremental output member when the actuator is moved past the end configuration. The formation may comprise a bumped up portion of an otherwise generally straight surface against which the actuator engages and along which it is arranged to slide during a canister firing sequence.

The dose counter may include a counter pawl, the counter pawl having a tooth arranged to engage the incremental

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output member, the tooth and incremental output member being arranged to permit one way only incremental relative motion therebetween. When the incremental output member comprises a ratchet wheel, the tooth can therefore serve as an anti-back drive tooth for the ratchet wheel, thereby permitting only one way motion or rotation thereof.

The counter pawl may be substantially fixedly mounted on the main body of the incremental count system and the counter pawl may be arranged to be capable of repeatedly engaging equi-spaced teeth of the incremental output member in anti-back drive interlock configurations as the counter is operated. The counter pawl may be positioned so that the incremental output member is halfway, or substantially halfway moved from one anti-back drive interlock configuration to the next when the actuator and incremental output member are in the end configuration thereof. This is highly advantageous in that it minimises the risk of double counting or non-counting by the dose counter.

According to a further aspect of the invention there is provided an inhaler comprising a main body arranged to retain a medicament canister of predetermined configuration and a dose counter mounted in the main body.

The inhaler main body may include a canister receiving portion and a separate counter chamber, the dose counter being located within the main body thereof, the incremental output member and actuator thereof inside the counter chamber, the main body of the inhaler having wall surfaces separating the canister-receiving portion and the counter chamber, the wall surfaces being provided with a communication aperture, an actuation member extending through the communication aperture to transmit canister motion to the actuator.

According to a further aspect of the present invention there is a provided an inhaler for metered dose inhalation, the inhaler comprising a main body having a canister housing arranged to retain a medicament canister for motion therein, and a dose counter, the dose counter having an actuation member having at least a portion thereof located in the canister housing for operation by movement of a medicament canister, wherein the canister housing has an inner wall, and a first inner wall canister support formation located directly adjacent the actuation member.

This is highly advantageous in that the first inner wall canister support formation can prevent a canister from rocking too much relative to the main body of the inhaler. Since the canister may operate the actuation member of the dose counter, this substantially improves dose counting and avoids counter errors.

The canister housing may have a longitudinal axis which passes through a central outlet port thereof, the central outlet port being arranged to mate with an outer canister fire stem of a medicament canister, the inner wall canister support formation, the actuation member and the outlet port lying in a common plane coincident with the longitudinal axis. Accordingly, this construction may prevent the canister from rocking towards the position of the dose counter actuation member, thereby minimising errors in counting.

The canister housing may have a further inner canister wall support formation located on the inner wall opposite, or substantially opposite, the actuation member. Accordingly, the canister may be supported against rocking motion away from the actuator member so as to minimise count errors.

The canister housing may be generally straight and tubular and may have an arrangement in which each said inner wall support formation comprises a rail extending longitudinally along the inner wall.

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Each said rail may be stepped, in that it may have a first portion located towards a medicine outlet end or stem block of the canister housing which extends inwardly a first distance from a main surface of the inner wall and a second portion located toward an opposite end of the canister chamber which extends inwardly a second, smaller distance from the main surface of the inner wall. This may therefore enable easy insertion of a canister into the canister housing such that a canister can be lined up gradually in step wise function as it is inserted into the canister housing.

The inhaler may include additional canister support rails which are spaced around an inner periphery of the inner wall of the canister housing and which extend longitudinally therealong.

At least one of the additional rails may extend a constant distance inwardly from the main surface of the inner wall.

At least one of the additional rails may be formed with a similar configuration to the first inner wall canister support formation.

The dose counter may, apart from said at least a portion of the actuation member, be located in a counter chamber separate from the canister housing, the actuation member comprising a pin extending through an aperture in a wall which separates the counter chamber and the canister housing.

According to a further aspect of the present invention there is provided an inhaler for inhaling medicaments having: a body for retaining a medicament store; the body including a dose counter, the dose counter having a moveable actuator and a return spring for the actuator, the return spring having a generally cylindrical and annular end; the body having a support formation therein for supporting said end of the return spring, the support formation comprising a shelf onto which said end is engageable and a recess below the shelf.

This shelf and recess arrangement is highly advantageous since it allows a tool (such as manual or mechanical tweezers) to be used to place the return spring of the actuator onto the shelf with the tool then being withdrawn at least partially via the recess.

The shelf may be U-shaped.

The support formation may include a U-shaped upstanding wall extending around the U-shaped shelf, the shelf and upstanding wall thereby forming a step and riser of a stepped arrangement.

The recess below the shelf may also be U-shaped.

At least one chamfered surface may be provided at an entrance to the shelf. This may assist in inserting the actuator and return spring into position.

A further aspect of the invention provides a method of assembly of an inhaler which includes the step of locating said end of said spring on the shelf with an assembly tool and then withdrawing the assembly tool at least partly via the recess. This assembly method is highly advantageous compared to prior art methods in which spring insertion has been difficult and in which withdrawal of the tool has sometimes accidentally withdrawn the spring again.

The cylindrical and annular end of the spring may be movable in a direction transverse to its cylindrical extent into the shelf while being located thereon.

According to a further aspect of the present invention there is provided an inhaler for inhaling medicament, the inhaler having a body for retaining a medicament store; and a dose counter, the dose counter having a moveable actuator and a chassis mounted on the body; the chassis being heat staked in position on the body. This is highly advantageous in that the chassis can be very accurately positioned

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and held firmly in place, thereby further improving counting accuracy compared to prior art arrangements in which some movement of the chassis relative to the body may be tolerated in snap-fit connections.

The chassis may have at least one of a pin or aperture heat staked to a respective aperture or pin of the body.

The chassis may have a ratchet counter output member mounted thereon.

The ratchet counter output member may comprise a ratchet wheel arranged to reel in incrementally a dose meter tape having a dosage indicia located thereon.

According to a further aspect of the present invention there is provided a method of assembling an inhaler including the step of heat staking the chassis onto the body. The step of heat staking is highly advantageous in fixedly positioning the chassis onto the body in order to achieve highly accurate dose counting in the assembled inhaler.

The method of assembly may include mounting a spring-returned ratchet actuator in the body before heat staking the chassis in place. The method of assembly may include pre-assembling the chassis with a dose meter tape prior to the step of heat staking the chassis in place. The method of assembly may include attaching a dose meter cover onto the body after the heat staking step. The cover may be welded onto the body or may in some embodiments be glued or otherwise attached in place.

According to a further aspect of the present invention there is provided an inhaler for inhaling medicament and having a body, the body have a main part thereof for retaining a medicament store; and a dose counter, the dose counter being located in a dose counter chamber of the body which is separated from the main part of the body, the dose counter chamber of the body having a dosage display and being perforated so as to permit the evaporation of water or aqueous matter in the dose counter chamber into the atmosphere.

This is highly advantageous since it enables the inhaler to be thoroughly washed and the dose counting chamber can thereafter dry out fully.

The display may comprise a mechanical counter display inside the dose counter chamber and a window for viewing the mechanical counter display. The mechanical counter display may comprise a tape. The perforated dose counter chamber may therefore enable reliable washing of the inhaler, if desired by the user, and may therefore dry out without the display window misting up.

The dose counter chamber may be perforated by a drain hole formed through an outer hole of the body. The drain hole may be located at a bottom portion of the body of the inhaler, thereby enabling full draining of the inhaler to be encouraged after washing when the inhaler is brought into an upright position.

According to a further aspect of the present invention there is provided a dose counter for an inhaler, the dose counter having a display tape arranged to be incrementally driven from a tape stock bobbin onto an incremental tape take-up drive shaft, the bobbin having an internal bore supported by and for rotation about a support shaft, at least one of the bore and support shaft having a protrusion which is resiliently biased into frictional engagement with the other of the bore and support shaft with longitudinally extending mutual frictional interaction. This arrangement may provide good friction for the bobbin, thereby improving tape counter display accuracy and preventing the bobbin from unwinding undesirably for example if the inhaler is accidentally dropped.

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The support shaft may be forked and resilient for resiliently biasing the support shaft and bore into frictional engagement.

The support shaft may have two forks, or more in some cases, each having a radially extending protrusion having a friction edge extending therealong parallel to a longitudinal axis of the support shaft for frictionally engaging the bore of the support shaft with longitudinally extending frictional interaction therebetween.

The bore may be a smooth circularly cylindrical or substantially cylindrical bore.

Each of the above inhalers in accordance with aspects of the present invention may have a medicament canister mounted thereto.

The canister may comprise a pressurised metered dose canister having a reciprocally movable stem extending therefrom and movable into a main canister portion thereof for releasing a metered dose of medicament under pressure, for example by operating a metered dose valve inside the canister body. The canister may be operable by pressing by hand on the main canister body.

In cases in which one or more support rails or inner wall support formations are provided, the canister may at all times when within the canister chamber have a clearance of about 0.25 to 0.35 mm from the first inner wall support formation. The clearance may be almost exactly 0.3 mm. This clearance which may apply to the canister body itself or to the canister once a label has been applied, is enough to allow smooth motion of the canister in the inhaler while at the same time preventing substantial rocking of the canister which could result in inaccurate counting by a dose counter of the inhaler, especially when lower face of the canister is arranged to engage an actuator member of the dose counter for counting purposes.

According to a further aspect of the invention, a method of assembling a dose counter for an inhaler comprises the steps of providing a tape with dosing indicia thereon; providing tape positioning indicia on the tape; and stowing the tape while monitoring for the tape positioning indicia with a sensor. The method advantageously permits efficient and accurate stowing of the tape, e.g. by winding.

The dosing indicia may be provided as numbers, the tape positioning indicia may be provided as one or more lines across the tape. The stowing step comprises winding the tape onto a bobbin or shaft, and, optionally, stopping winding when the positioning indicia are in a predetermined position. The tape may be provided with pixelated indicia at a position spaced along the tape from the positioning indicia. The tape may also be provided with a priming dot.

According to a further aspect of the invention, a tape system for a dose counter for an inhaler has a main elongate tape structure, and dosing indicia and tape positioning indicia located on the tape structure. The tape positioning indicia may comprise at least one line extending across the tape structure. The tape system may comprise pixelated indicia located on the tape structure and spaced from the positioning indicia. The tape system may comprise a priming dot located on the tape structure. The positioning indicia may be located between the timing dot and the pixelated indicia. The main elongate tape structure may have at least one end thereof wound on a bobbin or shaft.

A further aspect of the invention provides a method of designing an incremental dose counter for an inhaler comprising the steps of calculating nominal canister fire and dose counter positions for a dose counter actuator of the inhaler; calculating a failure/success rate for dose counters built to tolerance levels for counting each fire of inhalers in

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which the dose counter actuators may be applied; and selecting a tolerance level to result in said failure/success rate to be at or below/above a predetermined value. This is highly advantageous in that it allows an efficient and accurate prediction of the reliability of a series of inhaler counters made in accordance with the design.

The method of designing may include selecting the failure/success rate as a failure rate of no more than one in 50 million. The method of designing may include setting an average count position for dose counters built to the tolerances to be at or after an average fire position thereof during canister firing motion. The method of designing may include setting the average count position to be about 0.4 to 0.6 mm after the average fire position, such as about 0.48 mm after. The method of designing may include setting tolerances for the standard deviation of the fire position in dose counters built to the tolerances to be about 0.12 to 0.16 mm, such as about 0.141 mm. The method of designing may include setting tolerances for the standard deviation of the count positions in dose counters built to the tolerances to be about 0.07 to 0.09 mm, such as about 0.08 mm. A further aspect of the invention provides a computer implemented method of designing an incremental dose counter for an inhaler which includes the aforementioned method of designing.

A further aspect of the invention provides a method of manufacturing in a production run a series of incremental dose counters for inhalers which comprises manufacturing the series of dose counters in accordance with the aforementioned method of designing.

A further aspect of the invention provides a method of manufacturing a series of incremental dose counters for inhalers, which comprises manufacturing the dose counters with nominal canister fire and dose count positions of a dose counter actuator relative to a dose counter chassis (or inhaler main body), and which includes building the dose counters with the average dose count position in the series being, in canister fire process, at or after the average canister fire position in the series.

According to a further aspect of the invention, the method provides fitting each dose counter in the series of incremental dose counters to a corresponding main body of an inhaler.

These aspects advantageously provide for the production run of a series of inhalers and dose counters which count reliably in operation.

According to a further aspect of the invention, an incremental dose counter for a metered dose inhaler has a body arranged to retain a canister for movement of the canister relative thereto, the incremental dose counter having a main body, an actuator arranged to be driven and to drive an incremental output member in a count direction in response to canister motion, the actuator being configured to restrict motion of the output member in a direction opposite to the count direction. This advantageously enables an inhaler dose counter to keep a reliable count of remaining doses even if dropped or otherwise jolted.

The output member may comprise a ratchet wheel. The actuator may comprise a pawl and in which the ratchet wheel and pawl are arranged to permit only one-way ratcheting motion of the wheel relative to the pawl. The dose counter may include an anti-back drive member fixed to the main body. In a rest position of the dose counter, the ratchet wheel is capable of adopting a configuration in which a back surface of one tooth thereof engages the anti-back drive member and the pawl is spaced from an adjacent back

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surface of another tooth of the ratchet wheel without positive drive/blocking engagement between the pawl and wheel.

BRIEF DESCRIPTION OF THE DRAWINGS

The present invention may be carried out in various ways and preferred embodiment of a dose counter, inhaler and methods of assembly, design and manufacture will now be described with reference to the accompanying drawings in which:

FIG. 1 is an isometric view of a main body of an embodiment of an inhaler related to the invention together with a mouthpiece cap therefor;

FIG. 2 is a top plan view of the components as shown in FIG. 1;

FIG. 3A is a section on the plane 3A-3A in FIG. 2;

FIG. 3B is a view corresponding to FIG. 3A but with a dose counter fitted to the main body of the inhaler;

FIG. 4A is an exploded view of the inhaler main body, mouthpiece cap, dose counter and a dose counter window;

FIG. 4B is a view in the direction 4B in FIG. 4C of a spring retainer of the dose counter;

FIG. 4C is a top view of the spring retainer of FIG. 4B;

FIG. 5 is a bottom view of the assembled inhaler main body, mouthpiece cap, dose counter and dose counter window;

FIGS. 6A, 6B, 6C, 6D, 6E, 6F, 6G and 6H are various views of dose counter components of the inhaler;

FIGS. 7A and 7B are sectional views showing canister clearance inside the main body of the inhaler;

FIG. 7C is a further sectional view similar to that of FIG. 7B but with the canister removed;

FIG. 7D is a top plan view of the inhaler main body;

FIGS. 8A, 8B, 8C and 8D show the inhaler main body and dose counter components during assembly thereof;

FIG. 9 shows a sectional side view of a datum line for an actuator pawl of the dose counter;

FIGS. 10A, 10B, 10C, 10D, 10E and 10F show various side views of positions and configurations of the actuator pawl, a ratchet wheel, and a count pawl;

FIG. 11 shows distributions for tolerances of start, reset, fire, count and end positions for the actuator of the dose counter;

FIG. 12 is an enlarged version of part of FIG. 4A;

FIG. 13 shows an end portion of a tape of the dose counter;

FIG. 14 shows a computer system for designing the dose counter;

FIG. 15 is an isometric view of a stock bobbin modified in accordance with the present invention for use in the dose counter of the inhaler of FIGS. 1 to 14;

FIG. 16 shows an end view of the stock bobbin of FIG. 15;

FIG. 17 is a section through a longitudinal axis of the stock bobbin of FIGS. 15 and 16;

FIGS. 18A, 18B and 18C are views of the stock bobbin of FIGS. 15 to 17 mounted in the dose counter chassis of FIGS. 1 to 14, with the control elements of the forks of the second shaft (or split pin) having a profile slightly different to that in FIG. 6F, with the forks in a compressed configuration;

FIGS. 19A, 19B and 19C are views equivalent to FIGS. 18A to 18C but with the forks in a more expanded configuration due to a different rotational position of the stock bobbin;

FIG. 20 is an isometric view of the chassis assembled and including the stock bobbin of FIGS. 15 to 17 but excluding the tape for reasons of clarity;

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FIG. 21 is a view of a preferred embodiment of a dry powder inhaler in accordance with the present invention;

FIG. 22 is an exploded view of the inhaler of FIG. 21;

FIG. 23 is a view of a dose counter of the inhaler of FIG. 21;

FIG. 24 is an exploded view of the dose counter shown in FIG. 23;

FIG. 25 is an exploded view of parts of the inhaler of FIG. 21; and

FIG. 26 is a view of a yoke of the inhaler of FIG. 21.

DETAILED DESCRIPTION OF THE INVENTION

FIG. 1 shows a main body 10 of a manually operated metered dose inhaler 12 in accordance with an embodiment related to the present invention and having a mouthpiece cap 14 securable over a mouthpiece 16 of the main body.

The main body has a canister chamber 18 into which a canister 20 (FIG. 7A) is slideable. The canister 20 has a generally cylindrical main side wall 24, joined by a tapered section 26 to a head portion 28 having a substantially flat lower face 30 which has an outer annular drive surface 32 arranged to engage upon and drive an actuation pin 34 of a dose counter 36 as will be described. Extending centrally and axially from the lower face 30 is a valve stem 38 which is arranged to sealingly engage in a valve stem block 40 of the main body 10 of the inhaler 12. The valve stem block 40 has a passageway 42 leading to a nozzle 44 for directing the contents of the canister 20, namely active drug and propellant, towards an air outlet 46 of the inhaler main body 12. It will be appreciated that due to gaps 48 between the canister 20 and an inner wall 50 of the main body 10 of the inhaler 12 an open top 52 of the main body 10 forms an air inlet into the inhaler 12 communicating via air passageway 54 with the air outlet 46, such that canister contents exiting nozzle 44 mix with air being sucked by the user through the air passageway 54 in order to pass together through the air outlet and into the mouth of the user (not shown).

The dose counter 36 will now be described. The dose counter 36 includes an actuation pin 34 biased upwardly from underneath by a return spring 56 once installed in the main body 10. As best shown in FIGS. 4A, 6H and 8A, the pin 34 has side surfaces 58, 60 arranged to slide between corresponding guide surfaces 62, 64 located in a dose counter chamber 66 of the main body 10, as well as an end stop surface 68 arranged to engage a corresponding end stop 70 formed in the dose counter chamber 66 to limit upward movement of the pin 34. The pin 34 has a top part 72 which is circularly cylindrical and extends through an aperture 74 formed through a separator wall 76 which separates the canister chamber 18 from the dose counter chamber 66. The top part 72 of the pin 34 has a flat top surface 78 which is arranged to engage the outer annular drive surface 32 of the canister 20.

The actuation pin 34 is integrally formed with a drive or actuator pawl 80. The actuator pawl 80 has a generally inverted U-shape configuration, having two mutually spaced and parallel arms 82, 84 extending from a base portion of the actuation pin 34, each holding at respective distal ends 88 thereof opposite ends of a pawl tooth member 90 which extends in a direction substantially perpendicular to the arms 82, 84, so as to provide what may be considered a "saddle" drive for pulling on each of the 11 drive teeth 92 of a ratchet wheel 94 of an incremental drive system 96 or ratchet mechanism 96 of the dose counter 36. As shown for example in FIG. 10B, the pawl tooth member 90 has a sharp lower

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longitudinal side edge 98 arranged to engage the drive teeth 92, the edge-to-surface contact provided by this engagement providing very accurate positioning of the actuator pawl 80 and resultant rotational positioning of the ratchet wheel 94.

The dose counter 36 also has a chassis preassembly 100 which, as shown in FIGS. 4A and 6A, includes a chassis 102 having a first shaft 104 receiving the ratchet wheel 94 which is secured to a tape reel shaft 106, and a second shaft (or split pin) 108 which is parallel to and spaced from the first shaft 104 and which slidably and rotationally receives a tape stock bobbin 110.

As shown in FIG. 6B, when the inhaler has not been used at all, the majority of a tape 112 is wound on the tape stock bobbin 110 and the tape 112 has a series of regularly spaced numbers 114 displayed therealong to indicate a number of remaining doses in the canister 20. As the inhaler is repeatedly used, the ratchet wheel 94 is rotated by the actuator pawl 80 due to operation of the actuation pin 34 by the canister 20 and the tape 112 is incrementally and gradually wound on to the tape reel shaft 106 from the second shaft 108. The tape 112 passes around a tape guide 116 of the chassis 102 enabling the numbers 114 to be displayed via a window 118 in a dose counter chamber cover 120 having a dose marker 132 formed or otherwise located thereon.

As shown in FIGS. 6A and 6D, the second shaft 108 is forked with two forks 124, 126. The forks 124, 126 are biased away from one another. The forks have located thereon at diametrically opposed positions on the second shaft 108 friction or control elements 128, 130, one on each fork. Each control element extends longitudinally along its respective fork 124, 126 and has a longitudinally extending friction surface 132, 134 which extends substantially parallel to a longitudinal axis of the second shaft and is adapted to engage inside a substantially cylindrical bore 136 inside the tape stock bobbin 110. This control arrangement provided between the bore 136 and the control elements 128, 130 provides good rotational control for the tape stock bobbin 110 such that it does not unwind undesirably such as when the inhaler is dropped. The tape force required to unwind the tape stock bobbin 110 and overcome this friction force is approximately 0.1 N.

As can be seen in FIG. 6D, as well as FIGS. 6G and 10A to 10F, the chassis 102 is provided with an anti-back drive tooth 138 or count pawl 138 which is resiliently and substantially fixedly mounted thereto. As will be described below and as can be seen in FIGS. 10A to 10F, when the actuation pin 34 is depressed fully so as to fire the metered valve (not shown) inside the canister 20, the actuator pawl 80 pulls down on one of the teeth 92 of the ratchet wheel 94 and rotates the wheel 94 anticlockwise as shown in FIG. 6D so as to jump one tooth 92 past the count pawl 138, thereby winding the tape 112 a distance incrementally relative to the dose marker 122 on the dose counter chamber 120 so as to indicate that one dose has been used.

With reference to FIG. 10B, the teeth of the ratchet wheel 94 have tips 143 which are radiused with a 0.1 mm radius between the flat surfaces 140, 142. The ratchet wheel 94 has a central axis 145 which is 0.11 mm above datum plane 220 (FIG. 9). A top/nose surface 147 of the anti-back drive tooth 138 is located 0.36 mm above the datum plane 220. The distance vertically (i.e. transverse to datum plane 220—FIG. 9) between the top nose surface 147 of the anti-back drive tooth is 0.25 mm from the central axis 145 of the wheel 94. Bump surface 144 has a lateral extent of 0.20 mm, with a vertical length of a flat 145' thereof being 1 mm, the width of the bump surface being 1.22 mm (in the direction of the axis 145), the top 149 of the bump surface 144 being 3.02

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mm vertically below the axis 145, and the flat 145' being spaced a distance sideways (i.e. parallel to the datum plane 220) 2.48 mm from the axis 145. The top surface 78 of the pin 34 (FIG. 6H) is 11.20 mm above the datum plane 220 (FIG. 9) when the actuator pawl 80 and pin 34 are in the start configuration. The length of the valve stem 22 is 11.39 mm and the drive surface 32 of the canister 20 is 11.39 mm above the datum plane 220 when the canister is at rest waiting to be actuated, such that there is a clearance of 0.19 mm between the canister 20 and the pin 34 in this configuration.

FIGS. 10A and 10B show the actuator pawl 80 and ratchet wheel 94 and count pawl 138 in a start position in which the flat top 78 of the pin 34 has not yet been engaged by the outer annular drive surface 32 of the canister 20 or at least has not been pushed down during a canister depression.

In this "start" position, the count pawl 138 engages on a non-return back surface 140 of one of the teeth 92 of the ratchet wheel 94. The lower side edge 98 of the actuator pawl is a distance "D" (FIG. 9) 1.33 mm above datum plane 220 which passes through bottom surface or shoulder 41 of valve stem block 40, the datum plane 220 being perpendicular to a main axis "X" of the main body 10 of the inhaler 12 which is coaxial with the centre of the valve stem block bore 43 and parallel to a direction of sliding of the canister 20 in the main body 10 of the inhaler 12 when the canister is fired.

As shown in FIG. 10B, an advantageous feature of the construction is that the pawl tooth/actuator 90 acts as a supplementary anti-back drive member when the inhaler 12 is not being used for inhalation. In particular, if the inhaler 12 is accidentally dropped, resulting in a jolt to the dose counter 36 then, if the wheel 94 would try to rotate clockwise (backwards) as shown in FIG. 10B, the back surface 140 of a tooth will engage and be blocked by the tooth member 90 of the pawl 80. Therefore, even if the anti-back drive tooth 138 is temporarily bent or overcome by such a jolt, undesirable backwards rotation of the wheel 94 is prevented and, upon the next canister firing sequence, the pawl 90 will force the wheel 94 to catch up to its correct position so that the dose counter 36 continues to provide correct dosage indication.

FIG. 10C shows a configuration in which the actuator pawl 80 has been depressed with the pin 34 by the canister 20 to a position in which the side edge 98 of the pawl tooth member 90 is just engaged with one of the teeth 92 and will therefore upon any further depression of the pin 34 begin to rotate the wheel 94. This is referred to as a "Reset" position or configuration. In this configuration, the lower side edge 98 of the actuator 80 is 0.64 mm above the datum plane 220.

FIG. 10D shows a configuration in which the actuator pawl 80 has been moved to a position lower than that shown in FIG. 10C and in which the metered dose valve (not shown) inside the canister has at this very position fired in order to eject active drug and propellant through the nozzle 44. It will be noted that in this configuration the count pawl 138 is very slightly spaced from the back surface 140 of the same tooth 92 that it was engaging in the configuration of FIG. 10D. The configuration shown in FIG. 10D is known as a "Fire" configuration. In this configuration the lower side edge 98 of the actuator 80 is 0.47 mm below the datum plane 220.

FIG. 10E shows a further step in the sequence, called a "Count" position in which the actuator pawl 80 has rotated the ratchet wheel 94 by the distance circumferentially angularly between two of the teeth 92, such that the count pawl 138 has just finished riding along a forward surface 142 of one of the teeth 92 and has resiliently jumped over the tooth

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into engagement with the back surface **140** of the next tooth. Accordingly, in this "Count" configuration, a sufficiently long stroke movement of the pin **34** has occurred that the tape **112** of the dose counter **36** will just have counted down one dose. In this configuration, the lower side edge **98** of the actuator is 0.95 mm below the datum plane **220**. Accordingly, in this position, the actuator **80** generally, including edge **98**, is 0.48 mm lower than in the fire configuration. It has been found that, although the count configuration happens further on than the fire configuration, counting is highly reliable, with less than 50 failed counts per million. This is at least partially due to momentum effects and to the canister releasing some back pressure on the user in some embodiments as its internal metering valve fires.

In the configuration of FIG. **10F**, the pawl **80** has been further depressed with the pin **34** by the canister **20** to a position in which it is just disengaging from one of the teeth **92** and the actuator pawl **80** is assisted in this disengagement by engagement of one of the arms **84** with a bump surface **144** on the chassis **102** (see FIG. **6G**) and it will be seen at this point of disengagement, which is called an "End" configuration, the count pawl **138** is positioned exactly halfway or substantially halfway between two of the drive teeth **92**. This advantageously means therefore that there is a minimum chance of any double counting or non-counting, which would be undesirable. In the end configuration, the side edge **98** of the actuator is 1.65 mm below the datum plane **220**. It will be appreciated that any further depression of the actuator pawl **80** and pin **34** past the "End" configuration shown in FIG. **10F** will have no effect on the position of the tape **112** displayed by the dose counter **36** since the actuator pawl **80** is disengaged from the ratchet wheel **94** when it is below the position shown in FIG. **10F**.

As shown in FIGS. **7C** and **7D**, the inner wall **50** of the main body **10** is provided with a two-step support rail **144** which extends longitudinally along inside the main body and is located directly adjacent the aperture **74**. As shown in FIG. **7B** a diametrically opposed two-step support rail **146** is also provided and this diametrically opposed in the sense that a vertical plane (not shown) can pass substantially directly through the first rail **144**, the aperture **74**, a central aperture **148** of the valve stem block **40** (in which canister stem **25** is located) and the second two-step support rail **146**. As shown in FIG. **7A** and schematically in FIG. **7B**, the rails **144**, **146** provide a maximum clearance between the canister **20** and the rails **144**, **146** in a radial direction of almost exactly 0.3 mm, about 0.25 to 0.35 mm being a typical range. This clearance in this plane means that the canister **20** can only rock backwards and forwards in this plane towards away from the actuation pin **34**. A relatively small distance and this therefore prevents the canister wobbling and changing the height of the actuation pin **34** as to undesirably alter the accuracy of the dose counter **36**. This is therefore highly advantageous.

The inner wall **50** of the main body **10** is provided with two further two-step rails **150** as well as two pairs **152**, **154** of rails extending different constant radial amounts inwardly from the inner wall **50**, so as to generally achieve a maximum clearance of almost exactly 0.3 mm around the canister **20** for all of the rails **144**, **146**, **150**, **152**, **154** spaced around the periphery of the inner wall **50**, in order to prevent undue rocking while still allowing canister motion freely inside the inhaler **12**. It will be clear from FIG. **7C** for example that the two-step rails have a first portion near an outlet end **156** of the canister chamber **18**, the first portion having a substantially constant radial or inwardly-extending width, a first step **160** leading to a second portion **162** of the rail, the

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second portion **102** having a lesser radial or inwardly extending extent than the first portion **156**, and finally a second step **164** at which the rail merges into the main inner wall **50** main surface.

A method of assembling the inhaler **12** will now be described.

With reference to FIG. **8A**, the main body **10** of the inhaler **12** is formed by two or more plastics mouldings which have been joined together to the configuration shown.

As shown in FIG. **8B**, the actuator pawl **80** and pin **34** are translated forward into position into a pin receiving area **166** in the dose counter chamber **66** and the pin **34** and actuator **80** may then be raised until the pin **34** emerges through the aperture **74**.

Next, the return spring **56** may be inserted below the pin **34** and a generally cylindrical annular lower end **168** of the spring **56** may be moved by a tweezer or tweezer-like assembly tool (not shown) into engagement with a shelf **170** of a spring retainer **172** in the dose counter chamber **66**. The spring retainer **172** is U-shaped and the shelf **170** is U-shaped and has a recess **174** formed below it. As shown in FIGS. **4B**, **4C** and **12** shelf **170** includes three chamfer surfaces **176**, **178**, **180** arranged to assist in moving the lower end of the spring **168** into position onto the shelf using the assembly tool (not shown). Once the lower end of the spring **168** is in place, the assembly tool (not shown) can easily be removed at least partly via the recess **174** below the lower end **168** of the spring **56**.

The tape **112** is attached at one end (not shown) to the tape stock bobbin **110** and is wound onto the bobbin by a motor **200** (FIG. **13**) having a hexagonal output shaft **202** which engages in a hexagonal socket **204** (FIG. **6B**) of the bobbin. During winding, the tape is monitored by a sensor **206**, which may be in the form of a camera or laser scanner, which feeds data to a computer controller **205** for the motor **200**. The controller **205** recognises three positioning markers **210** in the form of lines across the tape **112** and stops the motor **202** when the tape **112** is nearly fully wound onto the bobbin **110**, such that the distal end **212** of the tape **112** can be secured, e.g. by adhesive, to the tape reel shaft **106**. The controller **205** also recognises a pixelated tape size marker **214** observed by the sensor **206** and logs in a stocking system data store **217** details of the tape **112** such as the number of numbers **114** on the tape, such as one hundred and twenty or two hundred numbers **114**. Next, the tape reel shaft is wound until an appropriate position of the lines **210** at which a priming dot **216** will, once the bobbin **110** and reel shaft **106** are slid onto the second shaft **108** and second shaft **104**, be in a position to be located in the window **118** when the inhaler **12** is fully assembled. In the embodiments, the bobbin **110** and reel shaft **106** may be slid onto the shafts **108**, **104** before the tape **112** is secured to the reel shaft **106** and the reel shaft may then be wound to position the priming dot **216**.

Next, the assembled dose counter components of the chassis preassembly **100** shown in FIG. **6B** may as shown in FIG. **8C** be inserted into the dose counter chamber **66**, with pins **182**, **184**, **186** formed on the main body **10** in the dose counter chamber **66** passing through apertures or slots **188**, **190**, **192** formed on the chassis **102**, such that the pins **182**, **184**, **186** extend through (or at least into) the apertures or slots **188**, **190**, **192**. With the chassis **102** being relatively firmly pushed towards the main body **10**, the pins **182**, **184**, **186** are then heat staked and the chassis **102** is therefore after this held very firmly in position in the main body and is unable to move, thereby assisting in providing great accuracy for the dose counter **36**. Next, as shown in FIG. **8D**, the

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dose counter chamber cover **120** may be fitted over the dose counter chamber **66** and may be secured in place such as by welding, with the priming dot **216** being displayed through the window.

The user can, when readying the inhaler **12** for first use, prime the inhaler by depressing the canister **20** three times which will bring the first number **114** on the tape into display through the window **118** in place of the priming dot **216**, the number **114** shown in FIG. **8D** being “200”, thereby indicating that 200 doses are remaining to be dispensed from the canister **20** and inhaler **12**.

As shown in FIG. **8D**, and in FIG. **5**, an open drain hole **194** is provided at the bottom of the dose counter chamber **66** by a substantially semi-circular cut-out or recess formation **196** in a lower surface **198** of the main body **10** of the inhaler. Accordingly, if the user (not shown) should decide to wash the main body **10** of the inhaler, for example after encountering an unhygienic situation or simply as a matter of choice, the drain hole **194** allows initial draining of water from inside the dose counter chamber **66** and also thereafter evaporation of water or any aqueous matter in the dose counter chamber **66** so that the window **118** does not mist up undesirably.

FIG. **14** shows a computer system **230** for designing the dose counter **36** and in particular for calculating distributions representative of average positions and standard deviations in a production series of inhalers of the start, reset, fire, count and end positions of the actuator lower side edge **98** relative to the datum plane **220** (FIG. **9**) and therefore of the actuator pawl **80** generally relative to the ratchet wheel **94**, chassis **102** and, when the inhaler **12** is fully assembled, the main body **10** of the inhaler **12**. The computer system **230** includes a data store **232**, a CPU **234**, an input device **236** (such as a keyboard or communication port) and an output device **238** (such as a communications port, display screen and/or printer). A user may enter data via the input device **236** which may be used by the CPU **234** in a mathematical calculation to predict count failure rates when the various dose counters are to be built in a series with dose counter positions set with given averages and standard deviations and taking into account any momentum/inertia effects and metering valve user-back-pressure reduction effect which will occur upon canister firing of a given type of canister. The computer system **230** is thus mathematically used to design the distributions. For the inhaler **12** described herein with the dose counter **36** and canister **20**, the distributions are designed as shown in FIG. **11**. The x axis shows distance of the lower side surface **98** of the actuator **80** above the datum plane **220** and the y axis is representative of the distribution. Thus, curve **240** shows that the start configuration has an average 1.33 mm above the datum plane **200** (standard deviation is 0.1 mm), curve **242** shows that the reset configuration has an average of 0.64 mm above the datum plane **220** (standard deviation is 0.082 mm), curve **244** shows the fire configuration has an average 0.47 mm below the datum plane **220** (standard deviation is 0.141 mm), curve **246** shows the count configuration has an average 0.95 mm below the datum plane **220** (standard deviation is 0.080 mm), and curve **248** shows the end configuration has an average of 1.65 mm below the datum plane **220** (standard deviation is 0.144 mm).

FIGS. **15** to **20** show a version of the inhaler modified in accordance with the present invention. In these drawings, the same reference numerals have been used to those in the earlier drawings to denote the equivalent components. The inhaler **12** is the same as that in FIGS. **1** to **14** apart from the following modifications.

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First, it can be seen that there is a modification in that the drive teeth **92** of the ratchet wheel **94** have a different profile to that in FIGS. **1** to **14**. There are also only nine ratchet teeth **94** in this embodiment instead of eleven.

Additionally, as shown in FIGS. **18C** and **19C**, the control elements **128**, **130** on the forks **124**, **126** of the second shaft **108** have a tapered profile which is different to the profile of the control elements **128**, **130** shown in FIG. **6F**. Either profile can be used in the embodiment of FIGS. **15** to **20** however.

Furthermore, as shown in FIG. **15**, the tape stock bobbin **110** has an inwardly facing generally cylindrical engagement surface **300** with a wavelike form extending partially therealong. The engagement surface **300** has a cross-section **301** perpendicular to the longitudinal length of the stock bobbin **110** which is constant therealong. This cross-section **301** can be seen in FIG. **16** and consists of a series of ten regularly spaced concavities **302** and ten convex wall portions **304**. The convex wall portions **304** are equi-spaced between the concavities **302**. Each concavity **302** has a radius of 0.2 mm. Each convex wall portion **304** also has a radius of 0.2 mm. Finally, the cross section **301** also includes flat wall portions **306** between all of the radiused wall portions of the concavities **302** and convex wall portions **304**. The geometry of the cross-section **301** is therefore defined by the radii of the concavities **302** and convex wall portions **304**, the flat wall portions **306** and the fact that there are ten concavities **302** and convex wall portions **304**.

The minor diameter of the engagement surface **300**, i.e. between the tips of opposite convex wall portions **304**, is 2.46 mm. The major diameter of the engagement surface **300**, i.e. between the outermost portions of the concavities **302**, is 2.70 mm. The undeformed tip to tip maximum diameter of the forks **124**, **126** of the split pin (the second shaft) **108**, i.e. in the region of the maximum radial extent of the control elements **128**, **130**, is 3.1 millimeters and it will therefore be appreciated that the forks **124**, **126** are resiliently compressed once the stock bobbin **110** has been assembled onto the split pin **108** in all rotational configurations of the stock bobbin **110** relative to the split pin **108**. The minimum gap between the forks **124**, **126** in the plane of the cross sections of FIGS. **18C** and **19C** is 1 mm when the split pin **108** is in the undeformed, pre-inserted state. When the split pin **108** is at maximum compression, as shown in FIGS. **18A** to **18C** when the control elements **128**, **130** are shown to be engaged on top of the convex wall portions **304**, the gap **308** between the tips **310**, **312** of the forks **124**, **126** is 0.36 mm. On the other hand, when the split pin **108** is at minimum compression (once inserted into the stock bobbin) as shown in FIGS. **19A** to **19C**, when the control elements **128**, **130** rest in the concavities **302**, the gap between the tips **310**, **312** of the forks **124**, **126** is 0.6 mm. The control elements **128**, **130** are outwardly radiused with a radius also of 0.2 mm such that they can just rest on the concavities **302** with full surface contact (at least at an axial location on the split pin where the tapered control elements are at their maximum radial extent), without rattling in, locking onto or failing to fit in the concavities **302**. The radii of the control elements **128**, **130** is therefore preferably substantially the same as the radii of the concavities **302**.

It will be appreciated that whereas FIGS. **18B** and **19B** are end views along the coaxial axis of the stock bobbin **110** and split pin **108**, FIGS. **18A** and **19A** are cross-sections. FIG. **19A** is a section on the plane A-A' in FIG. **19C** and FIG. **18A** is a section at the same plane, but of course with the stock bobbin **110** rotated relative to the split pin **108**.

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As the inhaler 12 is used and the ratchet wheel 94 rotates in order to count used doses, the stock bobbin rotates incrementally through rotational positions in which rotation is resisted, i.e. due to increasing compression of the split pin 108 at such rotational positions, and rotational positions in which rotation is promoted, i.e. due to decreasing compression of the split pin 108 at such rotational positions and this may involve a click forward of the stock bobbin 110 to the next position equivalent to that in FIGS. 19A to 19C in which the control elements 128, 130 of the split pin art located in the concavities 302. This functionality firstly allows the stock bobbin to unwind during use as required, but also prevents the tape 112 from loosening during transit if the inhaler 12 is dropped, such as onto a hard surface. This is highly advantageous, since the tape 11 is prevented from moving to a position in which it will give an incorrect reading regarding the number of doses in the canister.

During compression and expansion of the forks in the radial direction between the two configurations shown in FIGS. 18C and 19C, the forks 124, 126 rotate about a point 316 on the split pin where the forks 124, 126 come together. This rotational action means that there is a camming action between the forks 124, 126 and the engagement surface 300 without significant friction but, nevertheless, the resilient forces provided by the regulator formed by the engagement surface 300 and forks 124, 126 are able to regulate unwinding of the tape such that it does not easily occur during transit or if the inhaler 12 is dropped. It has been found during testing that a force of 0.3 to 0.4 N needs to be applied to the tape 112 to overcome the regulator at the stock bobbin 110. 0.32 N is achieved with the control elements 128 having the profile shown in FIG. 19C and 0.38 N is achieved with the profile of the control elements 128 altered to be as shown as described with reference to FIG. 6F. These forces are substantially higher than the 0.1 N force mentioned above and undesirable movement of the tape is substantially avoided even if the inhaler is dropped onto a hard surface. The modified arrangement of FIGS. 15 to 20 does not provide this force "constantly" such that there is overall not an undesirably high friction of the tape 112 as it passes over the other components of the dose counter because, due to the incremental nature of the resilient forces at the regulator, the tape 112 can incrementally relax as it slides over the stationary chassis components.

Instead of having ten concavities 302 and convex wall portions 304, other numbers may be used, such as 8 or 12. However, it is preferred to have an even number, especially since two control elements 128, 130 are provided, so that all of the control elements 128, 130 will expand and contract simultaneously. However, other arrangements are envisaged with 3 or more forks and the number of concavities/convex wall portions may be maintained as an integer divisible by the number of forks to maintain a system with simultaneous expansion/contraction. For example, the use of 9, 12 or 15 concavities/convex wall portions with 3 forks is envisaged.

Instead of having the engagement surface 300 on the inside of the stock bobbin 110, it could be placed on the outside of the stock bobbin 110 so as to be engaged by flexible external legs/pawls or similar.

It will be noted that the regulator provided by the engagement surface 300 and forks 124, 126 does not only allow rotation of the stock bobbin in one direction as is the case with the ratchet wheel 94. Rotation in both directions is possible, i.e. forwards and backwards. This means that during assembly, the stock bobbin 110 can be wound backwards during or after fitting the bobbin 100, shaft 106 and tape 112 onto the carriage 102, if desired.

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The stock bobbin 110 and the carriage 102 including the split pin 108 are both moulded of polypropylene material.

It will be seen from FIG. 16 that the cross-sectional shape 301 is not symmetrical within the hexagonal socket 204. This has enabled the hexagonal socket 204 to be maintained at a useful size while still allowing the desired size and geometry of the cross section 301 to fit without interfering with the hexagonal shape of the hexagonal socket 204 and also permits moulding to work during manufacture.

As shown in FIG. 17, the stock bobbin 110 has a series of four circumferential ribs 330 inside it and a spaced therealong. These hold the stock bobbin 110 on the correct side of the mould tool during moulding.

FIGS. 21 and 22 show a preferred embodiment in accordance with the invention of an inhaler 510 for dispensing a dry-powdered medicament in metered doses for patient inhalation. The inhaler 510 is as disclosed in FIGS. 1 to 16 or EP-A-1330280, the contents of which are hereby fully incorporated herein by reference, but with the stock bobbin 110 and second shaft 108 of the dose counter 516 modified so as to be as in FIGS. 15 to 20 hereof. Thus, the dry powder inhaler 510 generally includes a housing 518, and an assembly 512 received in the housing (see FIG. 21). The housing 518 includes a case 520 having an open end 522 and a mouthpiece 524 (FIG. 25) for patient inhalation, a cap 526 secured to and closing the open end 522 of the case 520, and a cover 528 pivotally mounted to the case 520 for covering the mouthpiece 524. As shown in FIG. 22, the inhaler 510 also includes an actuation spring 569, first yoke 566 with opening 572, bellows 540 with crown 574, a reservoir 514, second yoke 568 with hopper 542 and dose counter 516 mounted thereto, and case 520 has transparent window 5130 thereon for viewing dose counter tape indicia 5128. The dose metering system also includes two cams 570 mounted on the mouthpiece cover 528 and movable with the cover 528 between open and closed positions. The cams 570 each include an opening 580 for allowing outwardly extending hinges 582 of the case 520 to pass therethrough and be received in first recesses 584 of the cover 528. The cams 570 also include bosses 586 extending outwardly and received in second recesses 588 of the cover 528, such that the cover 528 pivots about the hinges 582 and the cams 570 move with the cover 528 about the hinges 582. As described in EP-A-1330280, cams 570 act upon cam followers 578 to move second yoke 568 up and down and thereby operate dose counter by engagement of pawl 5138 on the second yoke 568 with teeth 5136. Remaining components of the inhaler are provided as, and operate as described, in EP-A-1330280.

The dose counting system 516 therefore includes a ribbon or tape 5128 (FIGS. 23 & 24), having successive numbers or other suitable indicia printed thereon, in alignment with a transparent window 5130 provided in the housing 18 (see FIG. 22). The dose counting system 516 includes the rotatable stock bobbin 110 (as described above), an indexing spool 5134 rotatable in a single direction, and the ribbon 5128 rolled and received on the bobbin 110 and having a first end 5127 secured to the spool 5134, wherein the ribbon 5128 unrolls from the bobbin 110 so that the indicia are successively displayed as the spool 5134 is rotated or advanced. In FIGS. 23 and 24 the wavelike engagement surface 300 of the bobbin 110 is not shown for the purposes of clarity.

The spool 134 is arranged to rotate upon movement of the yokes 566, 568 to effect delivery of a dose of medicament from reservoir 514, such that the number on the ribbon 5128 is advanced to indicate that another dose has been dispensed by the inhaler 510. The ribbon 5128 can be arranged such that the numbers, or other suitable indicia, increase or

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decrease upon rotation of the spool 5134. For example, the ribbon 5128 can be arranged such that the numbers, or other suitable indicia, decrease upon rotation of the spool 5134 to indicate the number of doses remaining in the inhaler 510. Alternatively, the ribbon 5128 can be arranged such that the numbers, or other suitable indicia, increase upon rotation of the spool 5134 to indicate the number of doses dispensed by the inhaler 10.

The indexing spool 5134 includes radially extending teeth 5136, which are engaged by pawl 5138 extending from a cam follower 578 of the second yoke 568 upon movement of the yoke to rotate, or advance, the indexing spool 5134. More particularly, the pawl 5138 is shaped and arranged such that it engages the teeth 5136 and advances the indexing spool 5134 only upon the mouthpiece cover 528 being closed and the yokes 566, 568 moved back towards the cap 526 of the housing 518.

The dose counting system 516 also includes a chassis 5140 that secures the dose counting system to the hopper 542 and includes shafts 108, 5144 for receiving the bobbin 110 and the indexing spool 5134. As described above with reference to FIGS. 1 to 20, the bobbin shaft 108 is forked and includes radially nubs 5146 for creating a resilient resistance to rotation of the bobbin 110 on the shaft 108 by engaging with the wavelike engagement surface 300 inside the bobbin 110. A clutch spring 5148 is received on the end of the indexing spool 5134 and locked to the chassis 5140 to allow rotation of the spool 5134 in only a single direction.

Various modifications may be made to the embodiment shown without departing from the scope of the invention as defined by the accompanying claims as interpreted under patent law.

What is claimed is:

1. A dose counter for a metered dose inhaler having a body arranged to retain a medicament canister of predetermined configuration for movement of the medicament canister relative thereto, the medicament canister containing an active drug; the dose counter comprising:

a ratchet wheel having a plurality of circumferentially spaced teeth,

an actuator comprising an actuator pawl arranged to engage with a first tooth of the ratchet wheel, wherein the actuator can be driven in response to canister motion to drive the ratchet wheel to rotate,

a count pawl arranged to engage with a second tooth of the ratchet wheel, wherein as the ratchet wheel is driven by the actuator to rotate, the count pawl rides along a forward surface of the second tooth and resiliently jumps over the second tooth, and

a dosage indicator associated with the count pawl, wherein the actuator is arranged to define a first reset position in which the actuator pawl is brought into engagement with the first tooth,

wherein the actuator is further arranged such that, during a canister fire sequence, when the actuator is in a second position, which is after the first reset position and at a canister fire configuration, the medicament canister fires medicament before the dose counter reaches a count configuration, and when the actuator is in a third position after the second position, the count pawl resiliently jumps over the second tooth and the dose counter reaches the count configuration, whereby the dosage indicator has indicated a count,

wherein, in the canister fire configuration, the actuator pawl is below a datum plane which passes through a shoulder of a valve stem block configured to receive the medicament canister.

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2. A dose counter as claimed in claim 1 in which the actuator is displaced less than 1 mm relative to the body between its locations in the canister fire and count configurations.

3. A dose counter as claimed in claim 1 wherein the dosage indicator includes a tape with incremental dose indicia located thereon, the tape being positioned on a tape stock bobbin and arranged to unwind therefrom.

4. The dose counter as claimed in claim 3, wherein the incremental dose indicia on the tape is in the form of even numbers and the body includes a dose marker that points to a location either at one of the even numbers or between two adjacent even numbers.

5. A dose counter as claimed in claim 1 in which the actuator and ratchet wheel are arranged to provide a start configuration at which the actuator is spaced from the ratchet wheel, and an end configuration at which the actuator disengages from the ratchet wheel during the canister fire sequence.

6. A dose counter as claimed in claim 5 in which:

(a) the actuator is arranged to be located about 1.5 to 2.0 mm from its location in the fire configuration when in the start configuration;

(b) the actuator is arranged to be located about 1.0 to 1.2 mm from its location in the fire configuration when in the reset configuration; or

(c) the actuator is arranged to be located about 1.1 to 1.3 mm from its location in the fire configuration when in the end configuration.

7. A dose counter as claimed in claim 5 in which the body includes a formation for forcing the actuator to disengage from the ratchet wheel when the actuator is moved past the end configuration.

8. A dose counter as claimed in claim 5 in which:

(a) the actuator is arranged to be located about 1.5 to 2.0 mm from its location in the fire configuration when in the start configuration;

(b) the actuator is arranged to be located about 1.0 to 1.2 mm from its location in the fire configuration when in the reset configuration; and

(c) the actuator is arranged to be located about 1.1 to 1.3 mm from its location in the fire configuration when in the end configuration.

9. A dose counter as claimed in claim 1, wherein the count pawl and the ratchet wheel are arranged to permit one way incremental relative motion therebetween.

10. A dose counter as claimed in claim 9 in which the actuator and ratchet wheel are arranged to provide a start configuration at which the actuator is spaced from the ratchet wheel, and an end configuration at which the actuator disengages from the ratchet wheel during the canister fire sequence and in which the count pawl is substantially fixedly mounted on the body and in which the count pawl is arranged to be capable of repeatedly engaging the teeth of the ratchet wheel in anti-back drive interlock configurations as the dose counter is operated, the count pawl being positioned so that the ratchet wheel is halfway, or substantially halfway, moved from one anti-back interlock configuration to the next when the actuator and ratchet wheel are in the end configuration thereof.

11. An inhaler comprising the body arranged to retain the medicament canister of predetermined configuration and the dose counter as claimed in claim 1.

12. An inhaler as claimed in claim 11 in which the body includes a canister-receiving portion and a separate counter chamber; the body, ratchet wheel and actuator being located inside the counter chamber, the body of the inhaler having

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wall surfaces separating the canister-receiving portion and the counter chamber, the wall surfaces being provided with a communication aperture, an actuation member extending through the communication aperture to transmit canister motion to the actuator.

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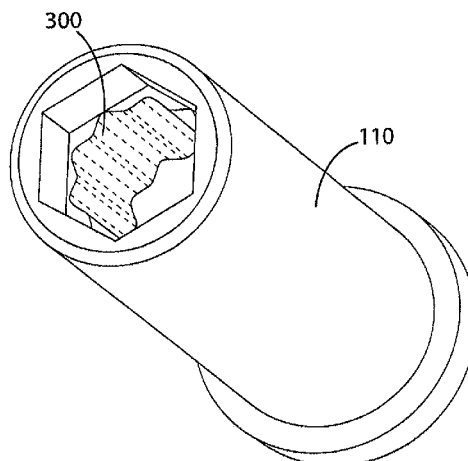
13. The dose counter of claim 1, wherein the shoulder is a bottom surface within the valve stem block and the datum plane is perpendicular to a direction of the movement of the medicament canister.

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* * * * *

EXHIBIT F

US010561808B2

(12) **United States Patent**
Walsh et al.(10) **Patent No.:** **US 10,561,808 B2**(45) **Date of Patent:** **Feb. 18, 2020**(54) **DOSE COUNTER FOR INHALER HAVING
AN ANTI-REVERSE ROTATION ACTUATOR**(71) Applicants: **IVAX PHARMACEUTICALS**
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Robert Charles Uschold, Leominster,
MA (US); **Jeffrey A. Karg**, Hopkinton,
MA (US)(73) Assignees: **IVAX PHARMACEUTICALS**
IRELAND, Waterford (IE); **NORTON**
(WATERFORD) LIMITED, Waterford
(IE); **TEVA PHARMACEUTICALS**
IRELAND, Waterford (IE)(*) Notice: Subject to any disclaimer, the term of this
patent is extended or adjusted under 35
U.S.C. 154(b) by 228 days.(21) Appl. No.: **15/262,818**(22) Filed: **Sep. 12, 2016**(65) **Prior Publication Data**
US 2016/0375208 A1 Dec. 29, 2016**Related U.S. Application Data**(60) Continuation of application No. 14/699,584, filed on
Apr. 29, 2015, which is a continuation of application
(Continued)(51) **Int. Cl.**
A61M 15/00 (2006.01)
G06M 1/24 (2006.01)
A61M 11/00 (2006.01)(52) **U.S. Cl.**
CPC **A61M 15/0078** (2014.02); **A61M 11/00**
(2013.01); **A61M 15/007** (2014.02);
(Continued)(58) **Field of Classification Search**
CPC **A61M 15/0078**; **A61M 15/0025**; **A61M**
15/0026; **A61M 15/007**; **A61M 15/0071**;
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(Continued)**OTHER PUBLICATIONS**Final Office Action dated Oct. 20, 2016 for U.S. Appl. No. 14/699,567.
(Continued)*Primary Examiner* — Daniel A Hess(74) *Attorney, Agent, or Firm* — Morgan, Lewis &
Bockius LLP(57) **ABSTRACT**A dose counter for an inhaler includes a counter display
arranged to indicate dosage information, and a drive system
arranged to move the counter display incrementally in a first
direction from a first station to a second station in response
to actuation input. A regulator is provided which is arranged
(Continued)

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Page 2

to act upon the counter display at the first station to regulate motion of the counter display at the first station to incremental movements.

29 Claims, 17 Drawing Sheets**Related U.S. Application Data**

- No. 14/103,353, filed on Dec. 11, 2013, now Pat. No. 9,526,850, which is a division of application No. 13/110,532, filed on May 8, 2011, now Pat. No. 8,978,966.
- (60) Provisional application No. 61/345,763, filed on May 18, 2010, provisional application No. 61/417,659, filed on Nov. 29, 2010.
- (52) **U.S. Cl.**
CPC *A61M 15/009* (2013.01); *A61M 15/0025* (2014.02); *A61M 15/0026* (2014.02); *A61M 15/0065* (2013.01); *A61M 15/0071* (2014.02); *G06M 1/246* (2013.01); *A61M 2202/064* (2013.01); *A61M 2205/6063* (2013.01); *A61M 2207/00* (2013.01); *A61M 2207/10* (2013.01); *Y10T 29/49* (2015.01); *Y10T 29/49764* (2015.01); *Y10T 29/49826* (2015.01)
- (58) **Field of Classification Search**
CPC A61M 11/00; A61M 15/0065; A61M 15/009; G06M 1/246
USPC 235/8
See application file for complete search history.

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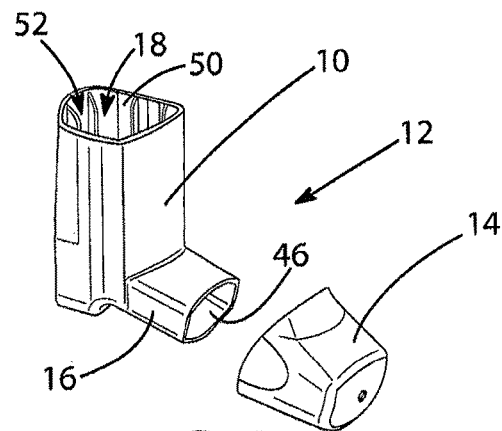


FIG. 1

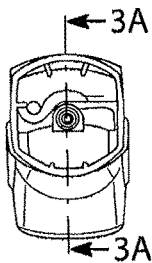


FIG. 2

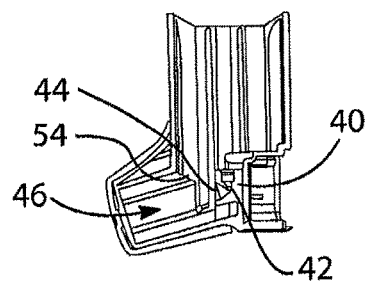


FIG. 3A

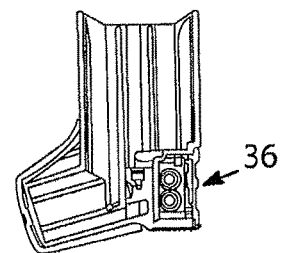


FIG. 3B

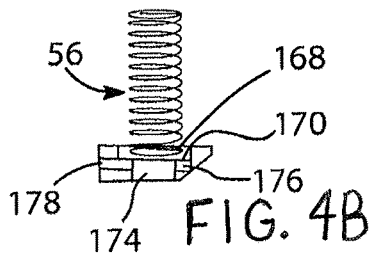


FIG. 4B

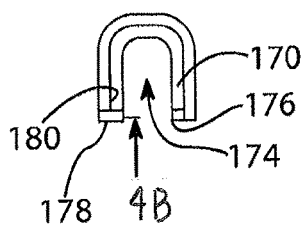


FIG. 4C

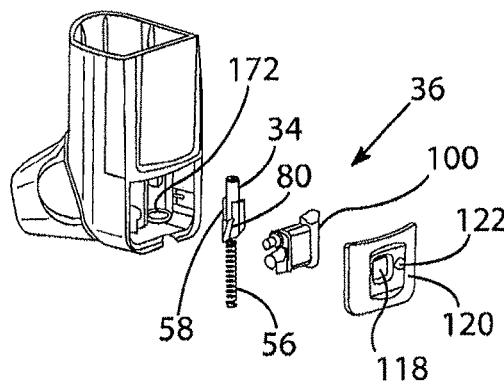


FIG. 4A

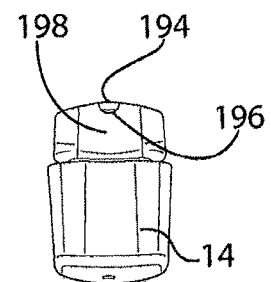


FIG. 5

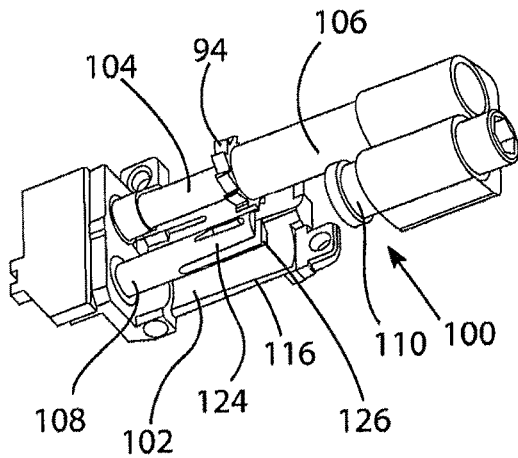


FIG. 6A

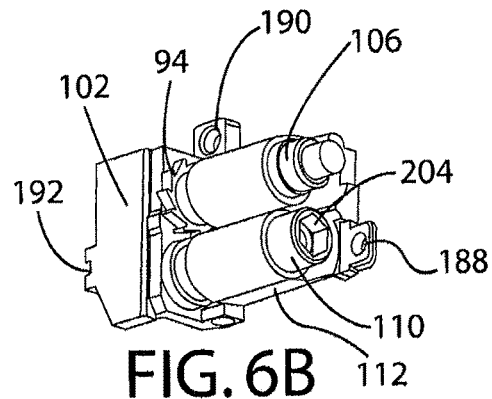


FIG. 6B

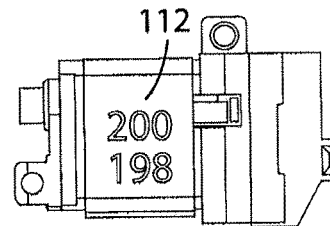


FIG. 6C

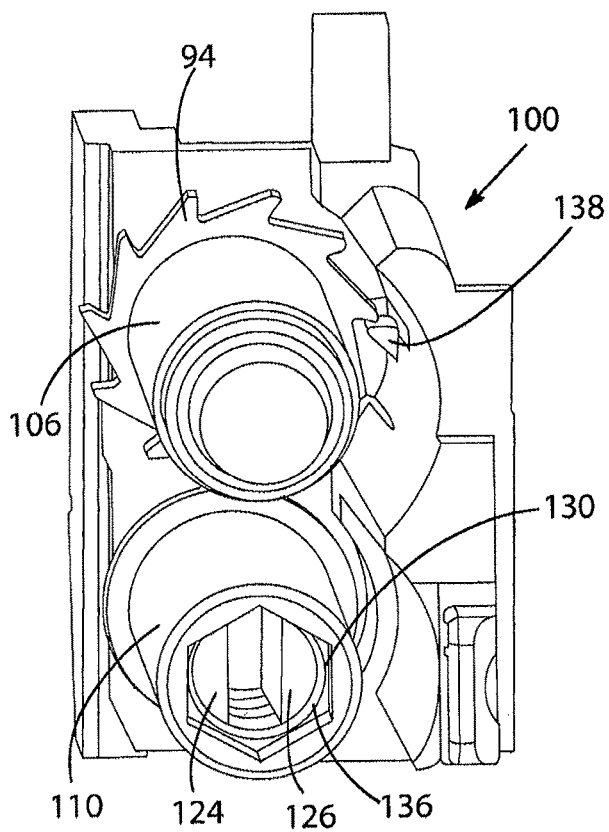


FIG. 6D

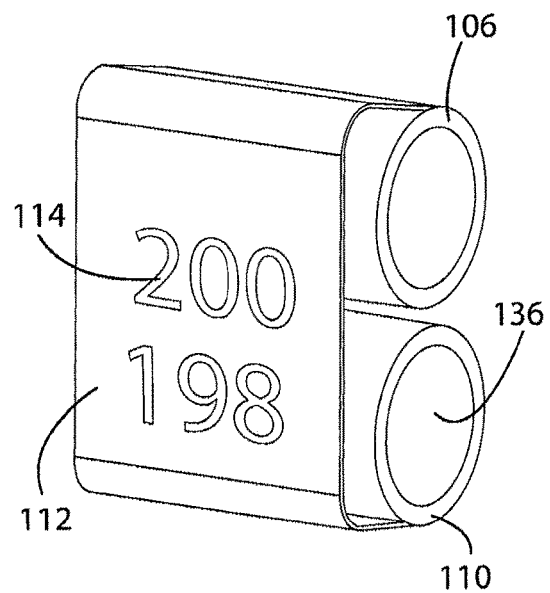


FIG. 6E

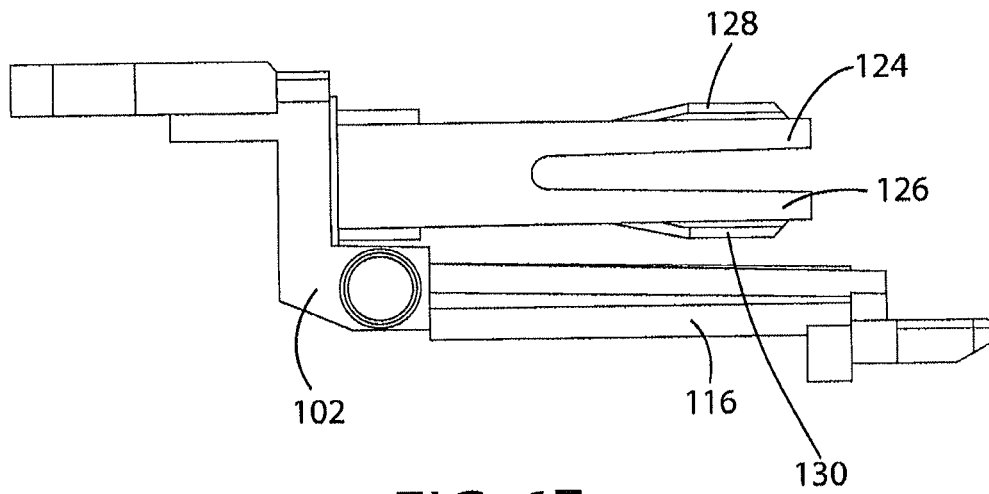


FIG. 6F

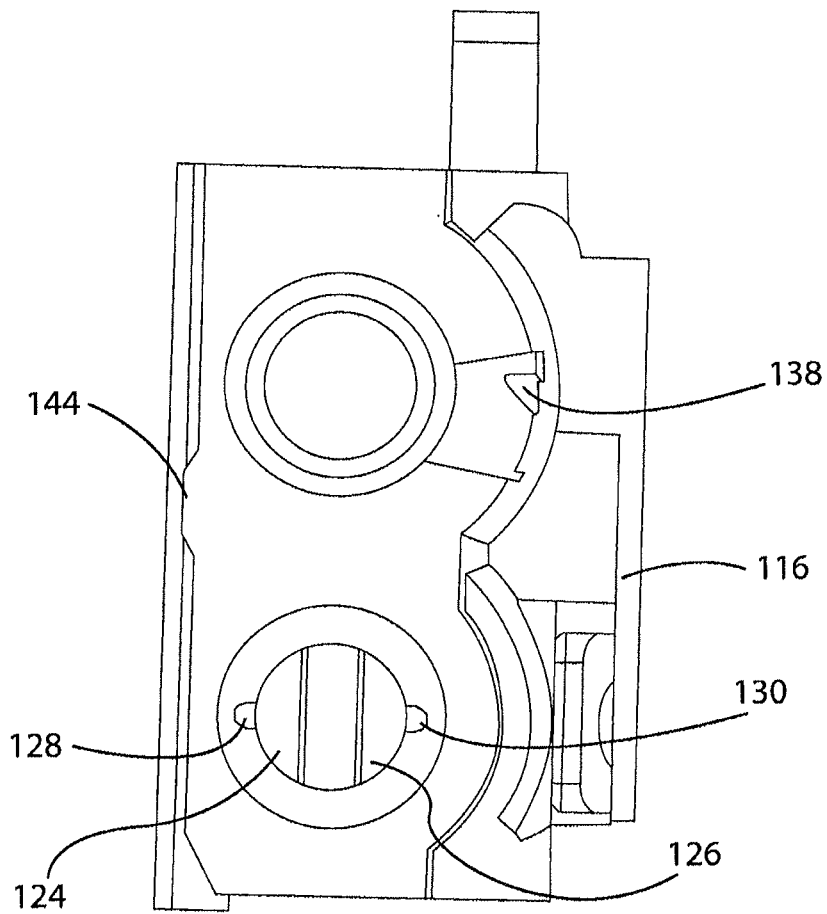


FIG. 6G

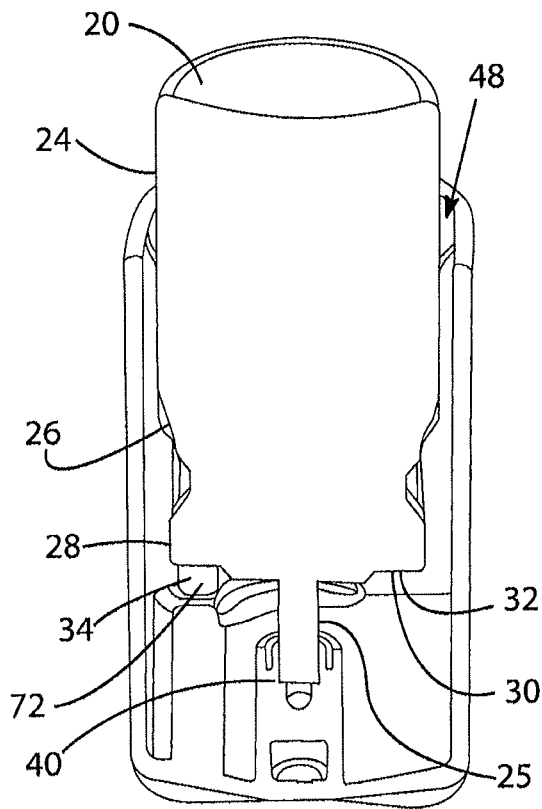


FIG. 7A

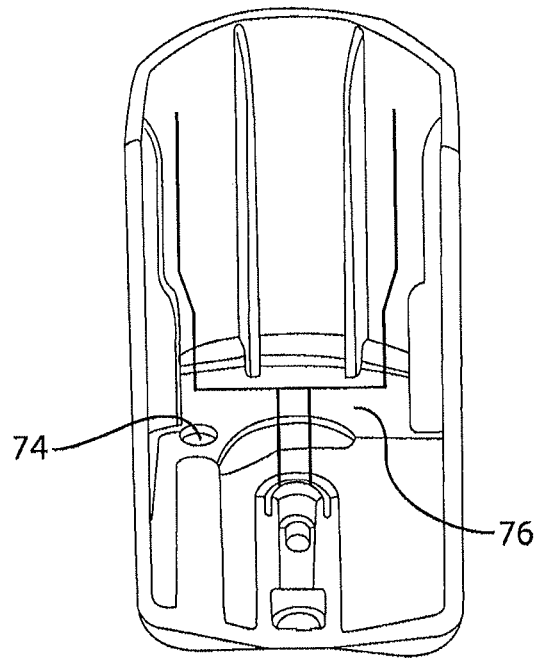


FIG. 7B

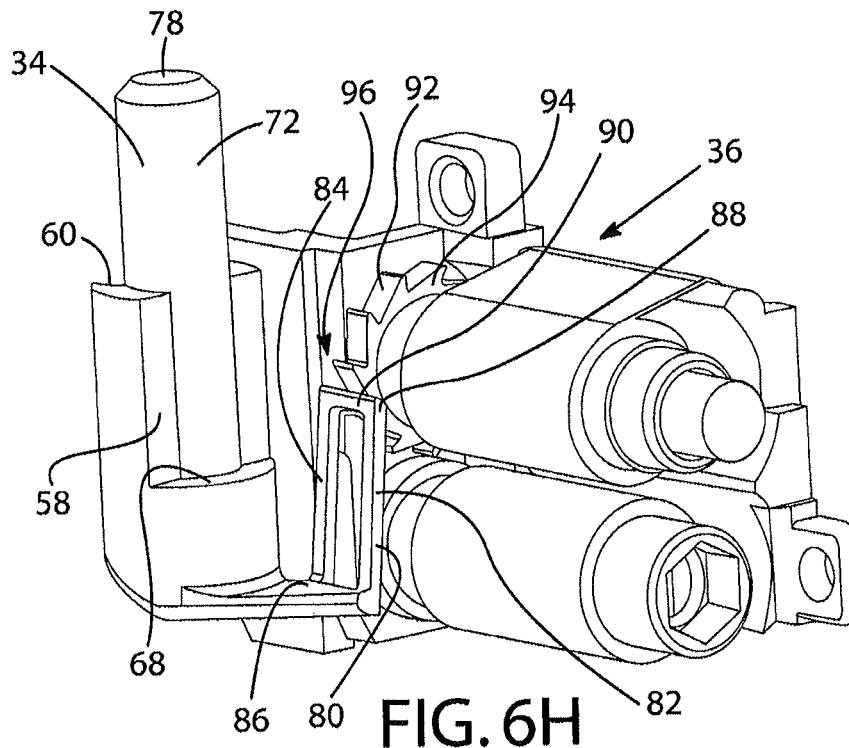


FIG. 6H

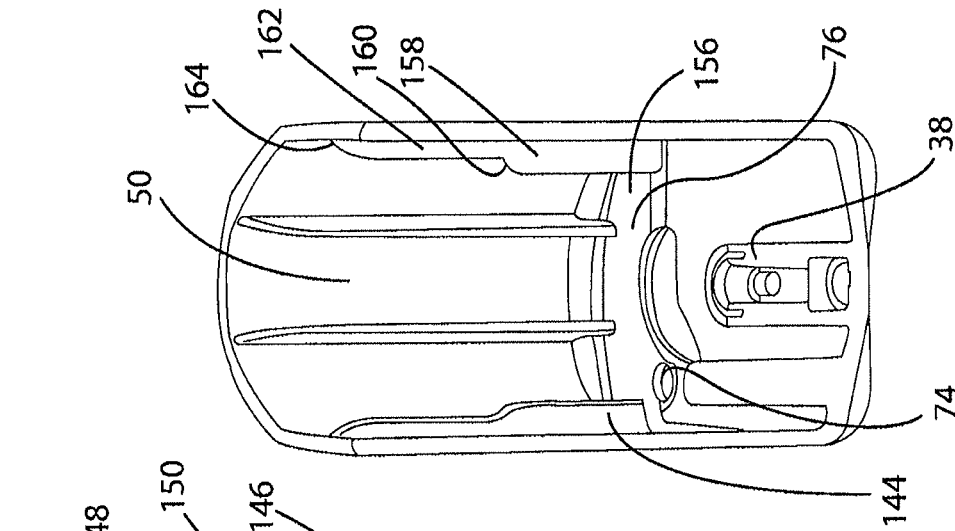


FIG. 7C

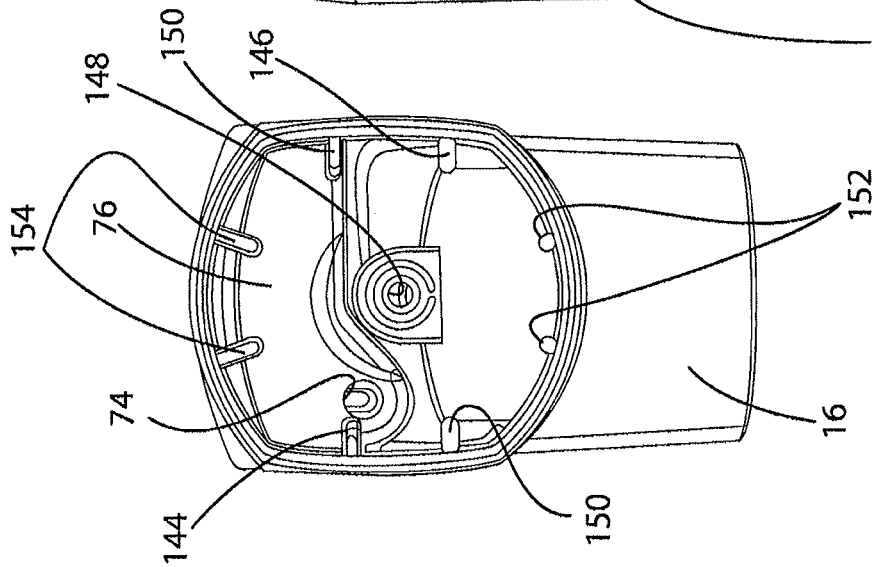


FIG. 7D

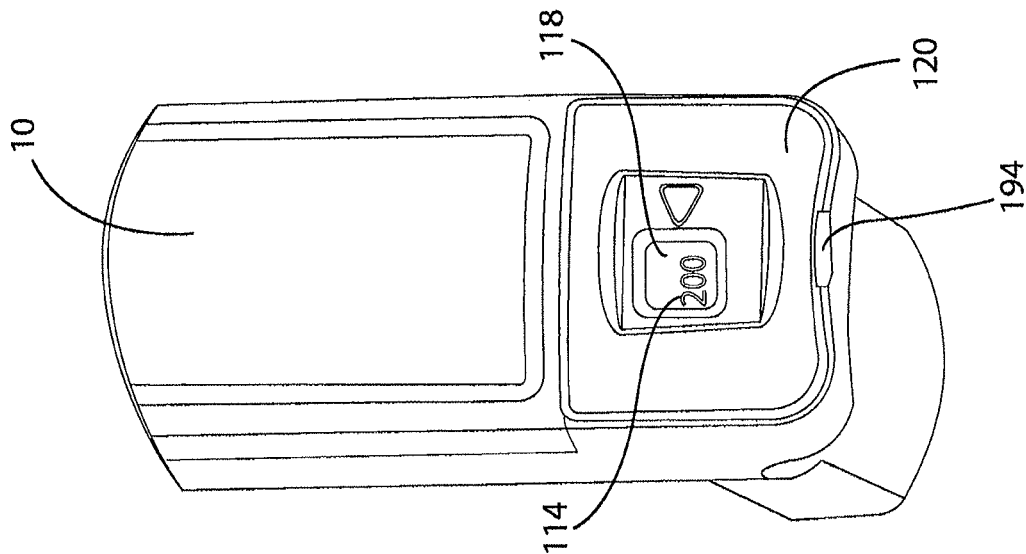


FIG. 8D

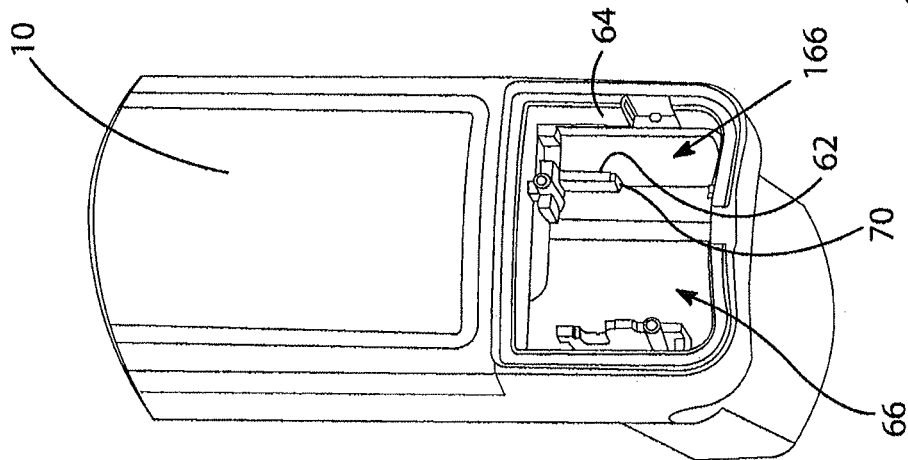


FIG. 8A

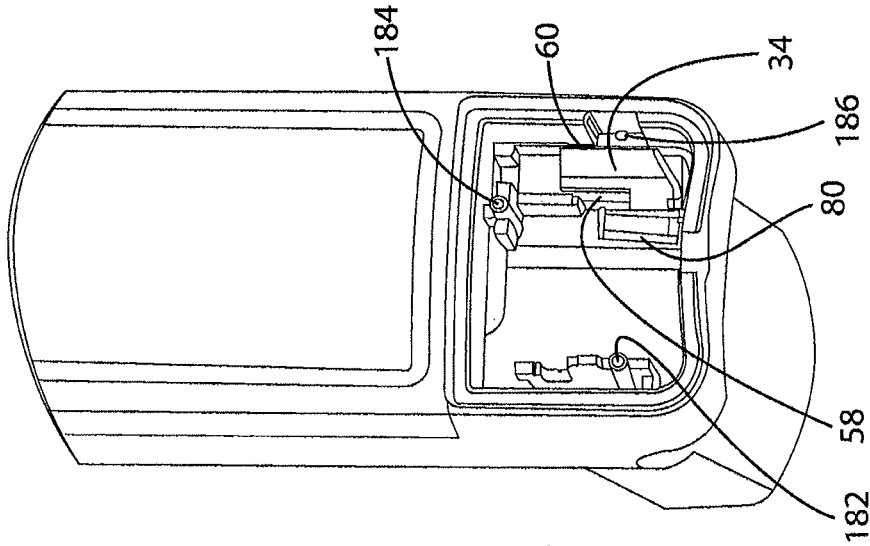


FIG. 8B

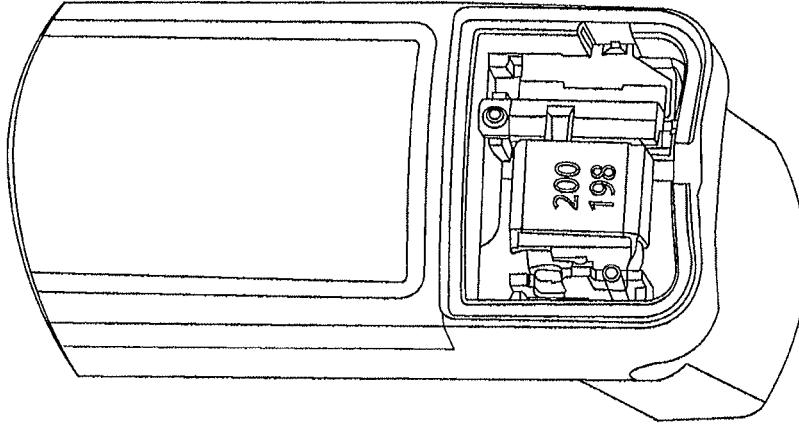


FIG. 8C

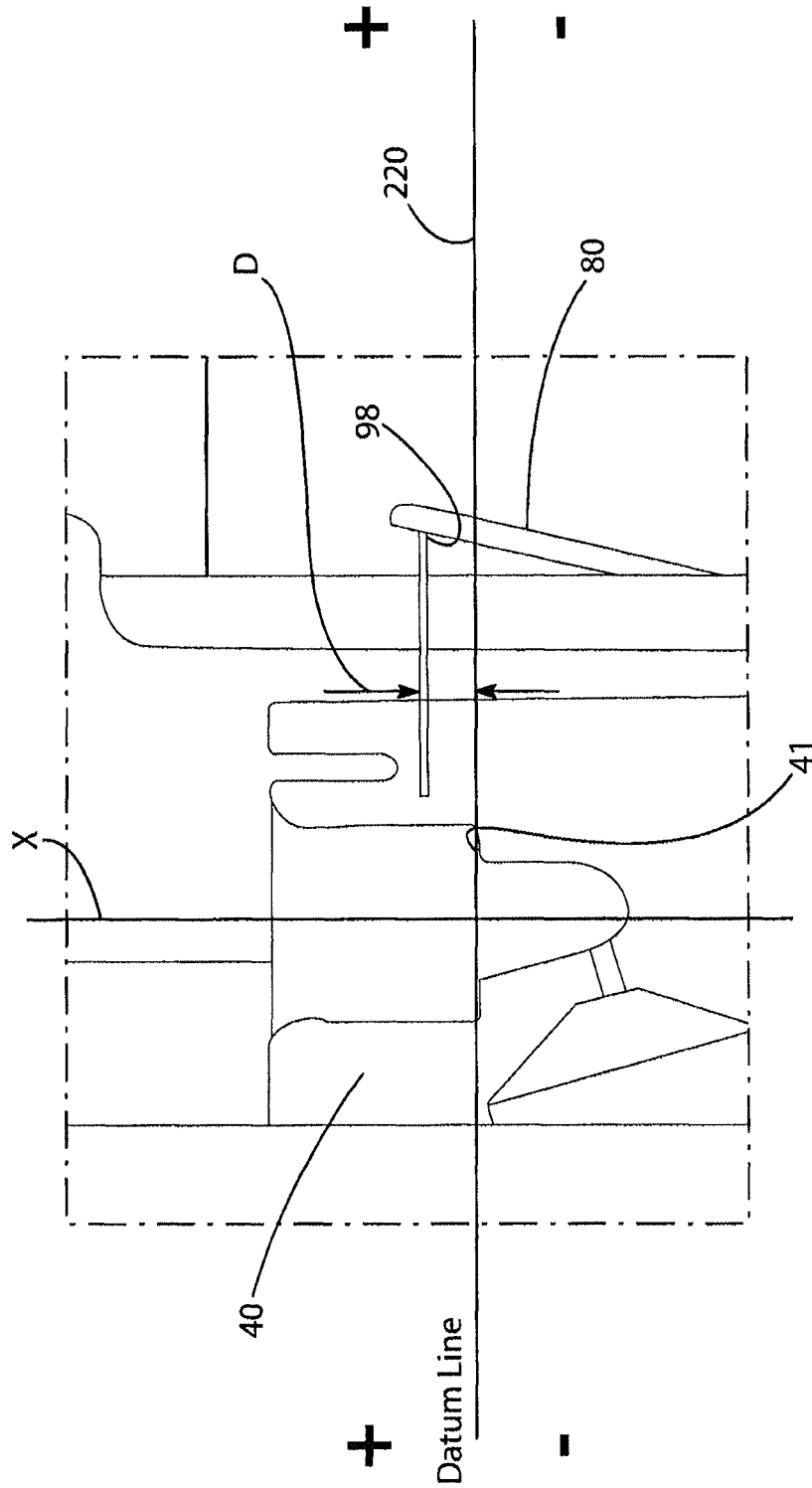
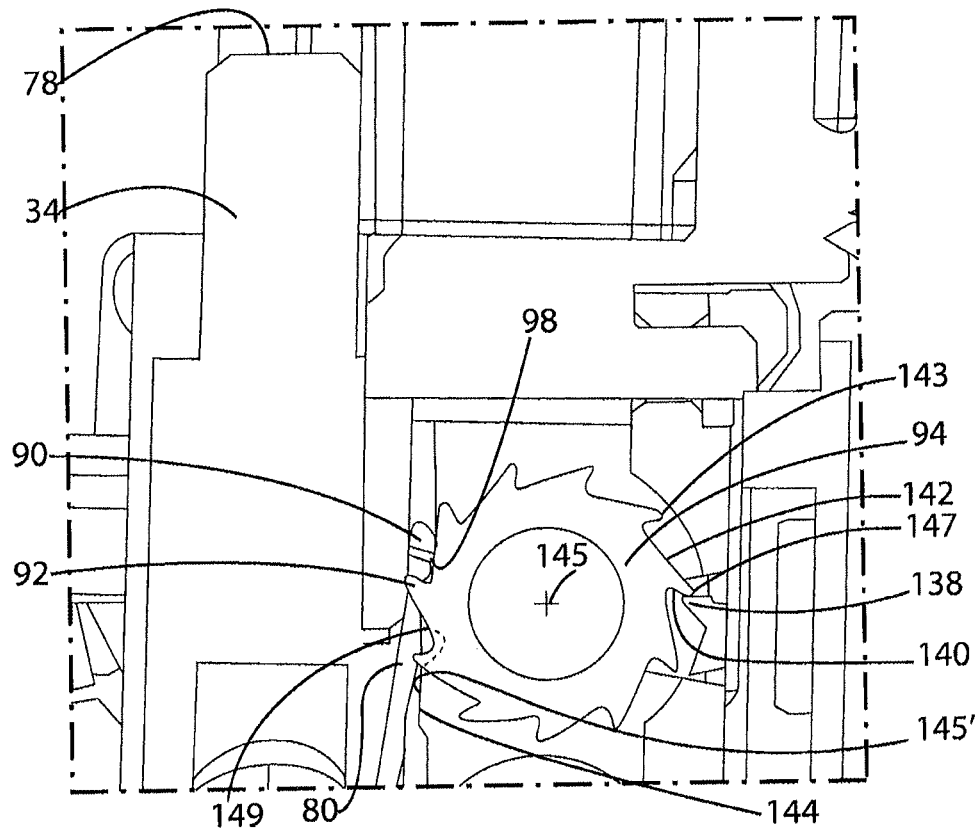
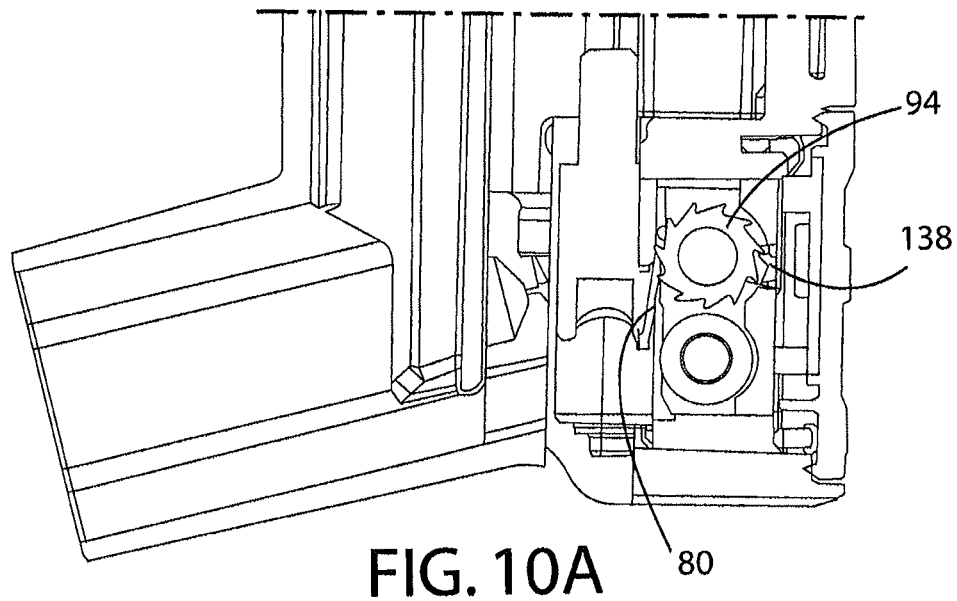


FIG. 9



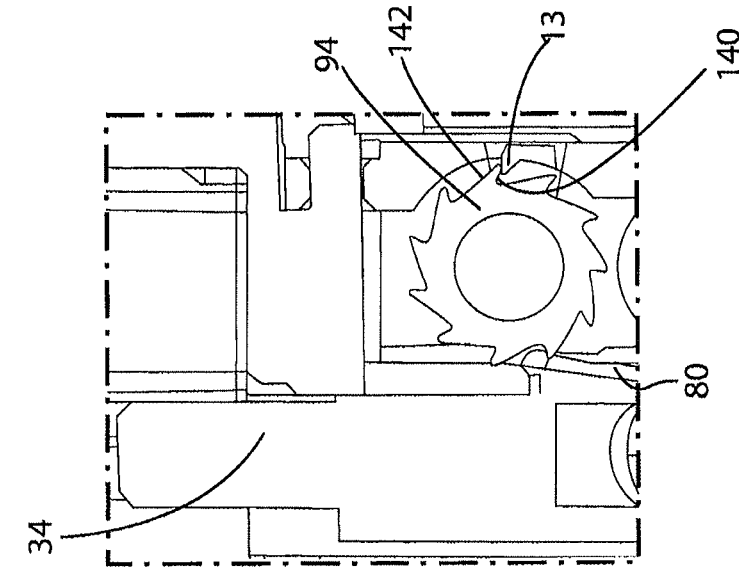


FIG. 10C

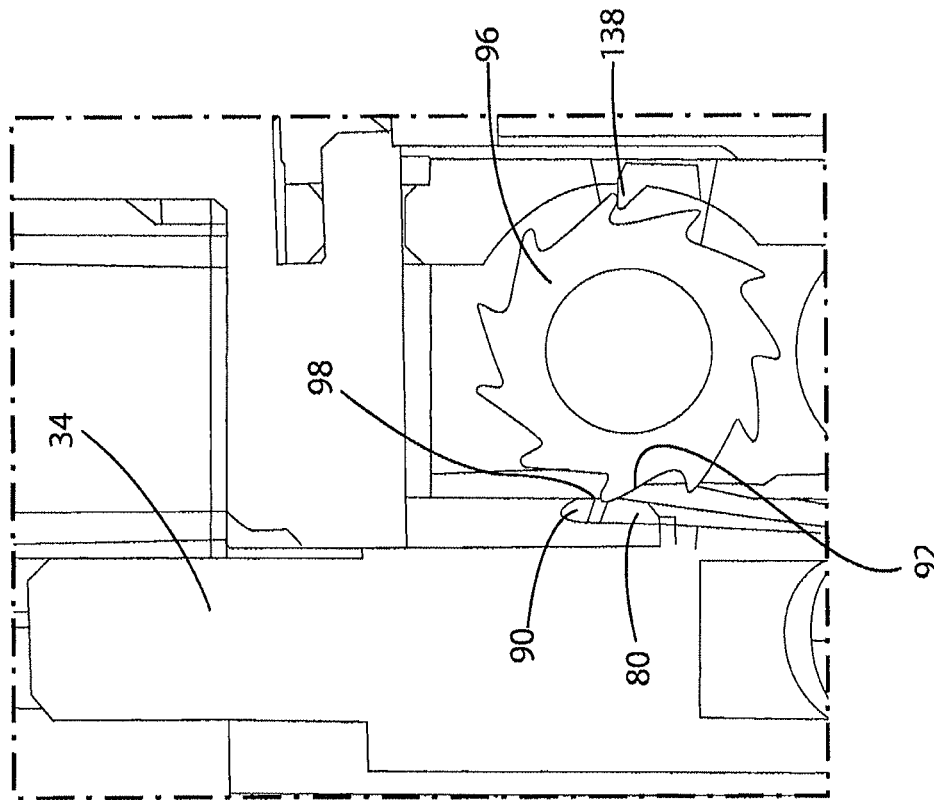


FIG. 10E

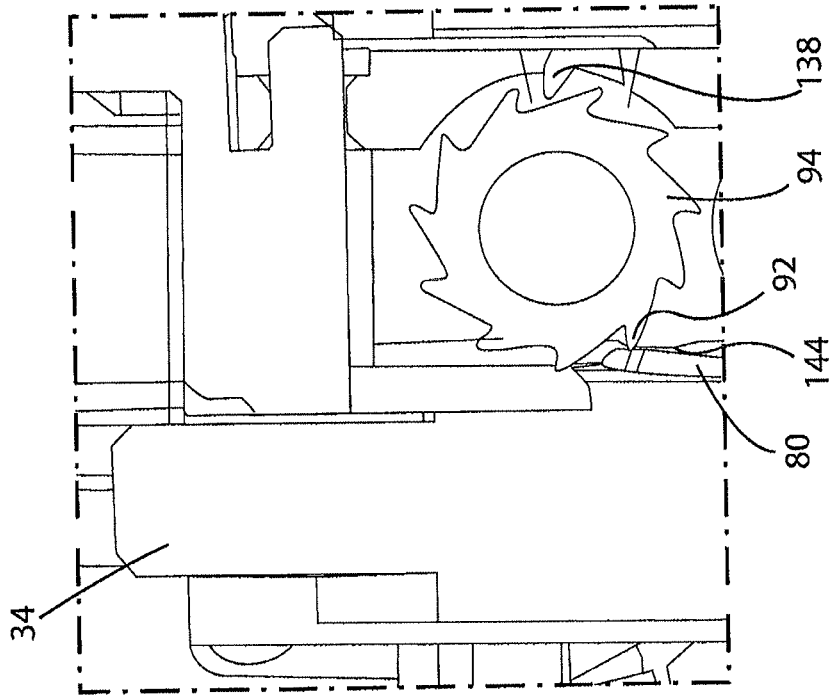


FIG. 10F

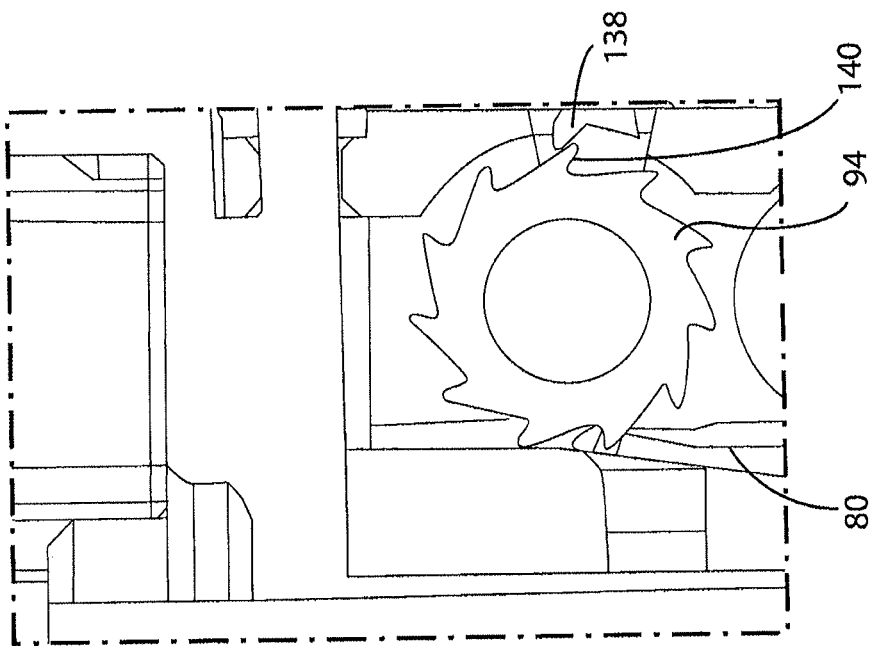


FIG. 10D

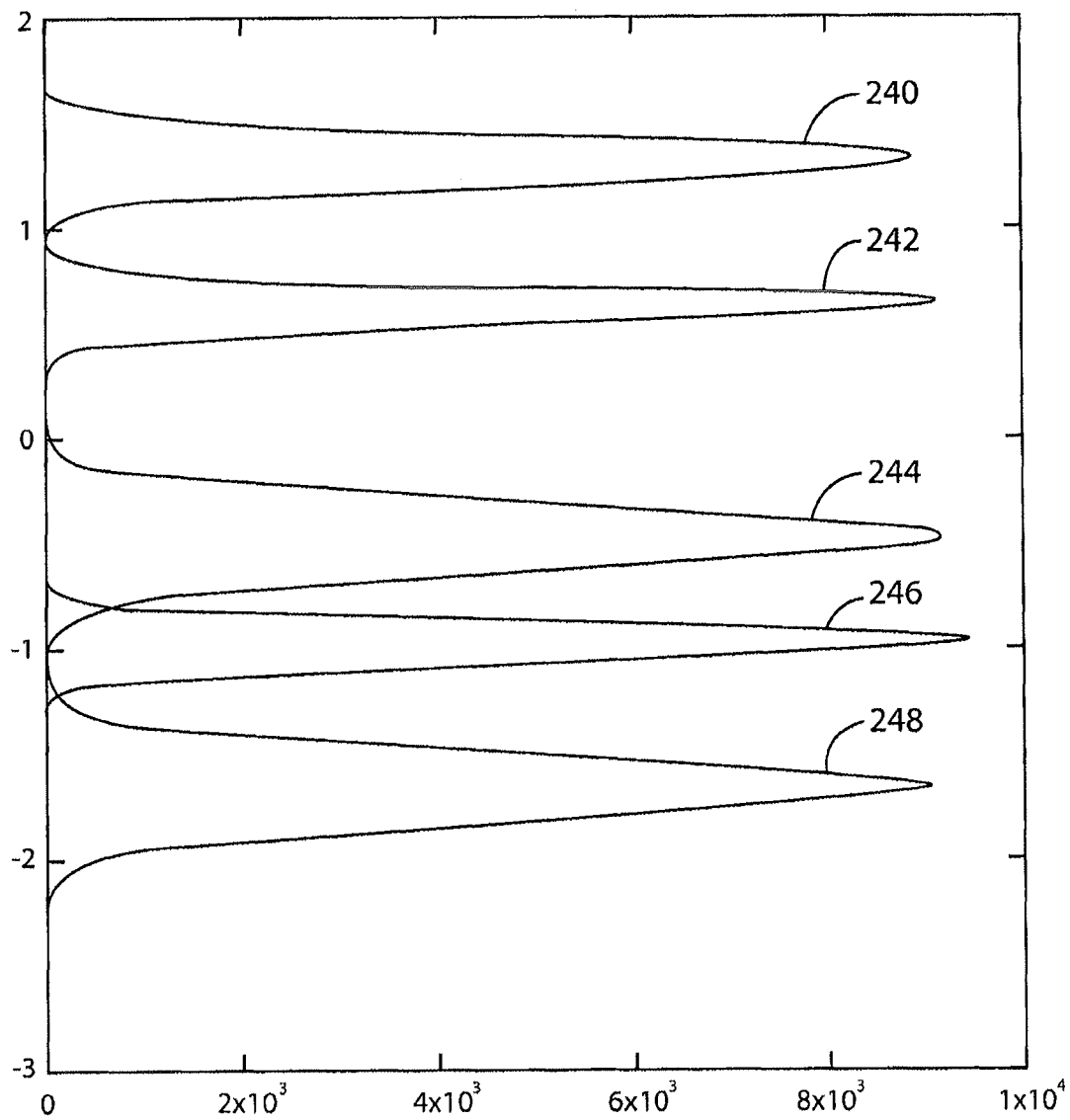


FIG. 11

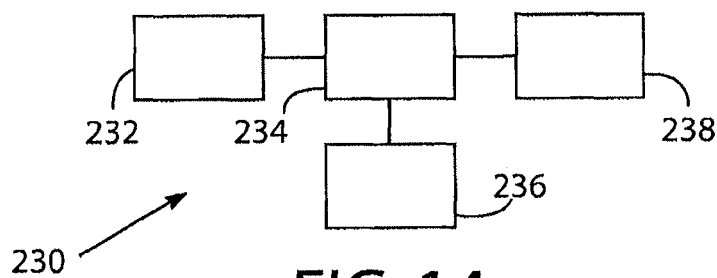


FIG. 14

U.S. Patent

Feb. 18, 2020

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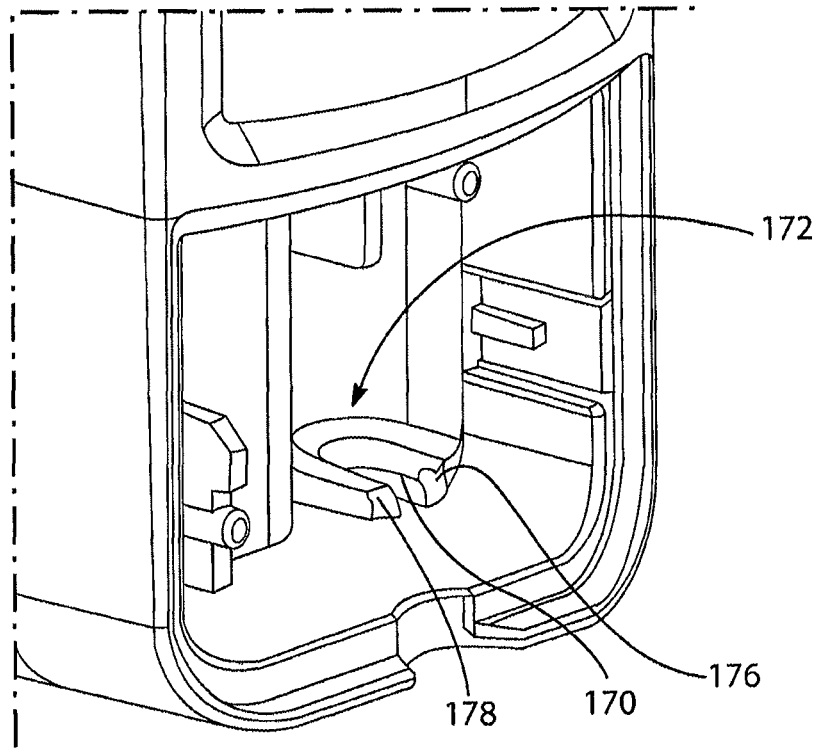


FIG. 12

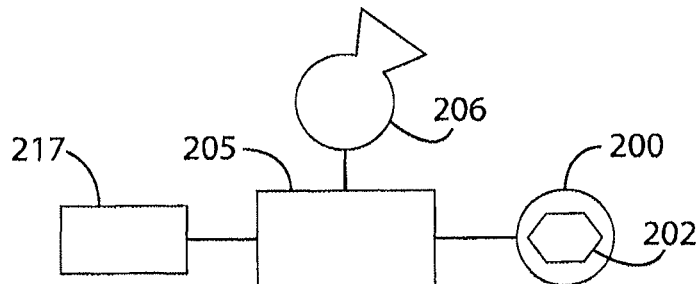
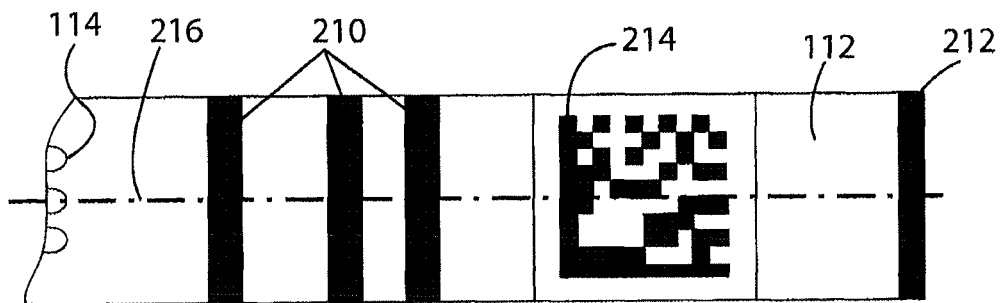


FIG. 13

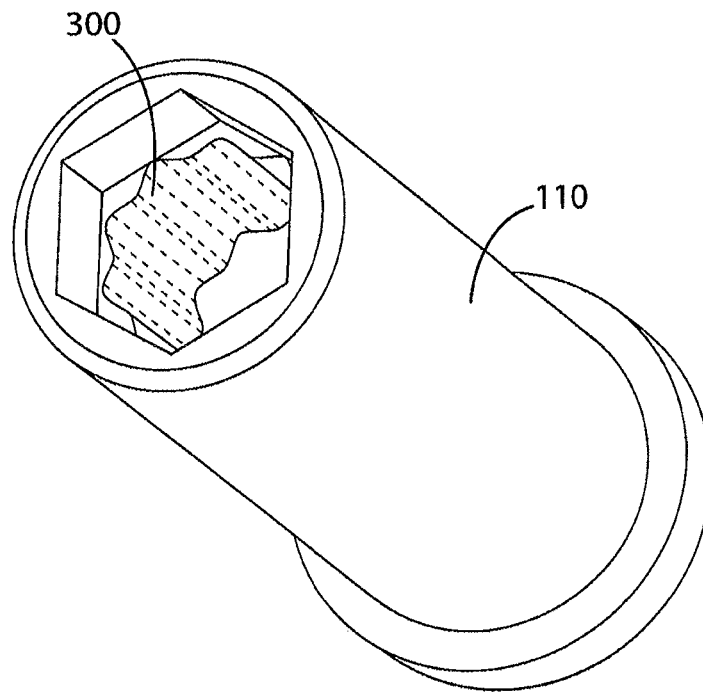


FIG. 15

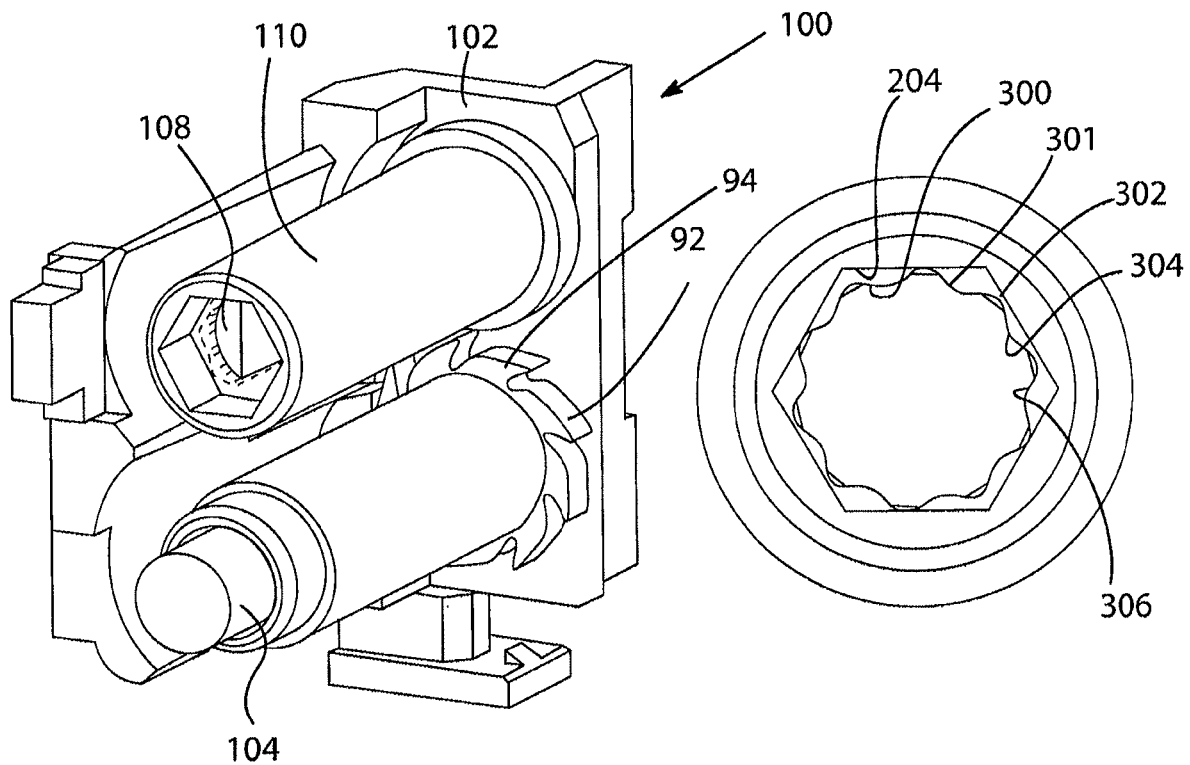


FIG. 20

FIG. 16

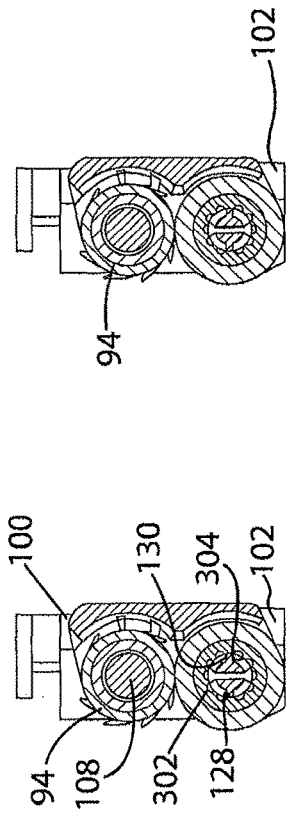


FIG. 18A

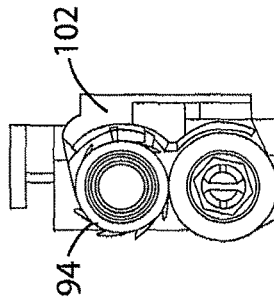


FIG. 18B

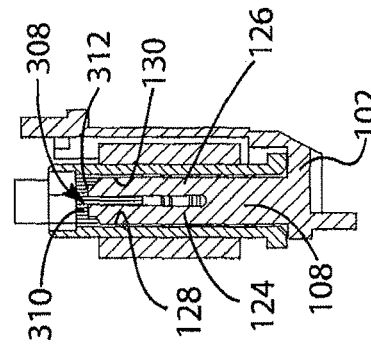


FIG. 18C

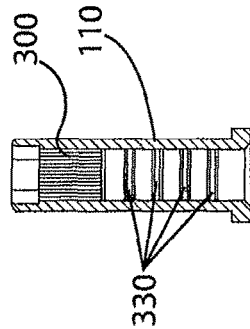


FIG. 17

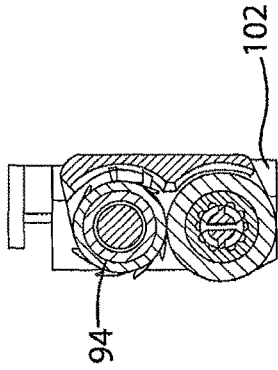


FIG. 19A

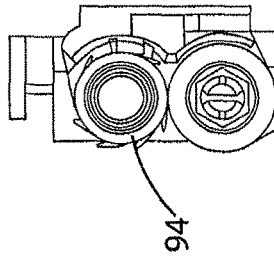


FIG. 19B

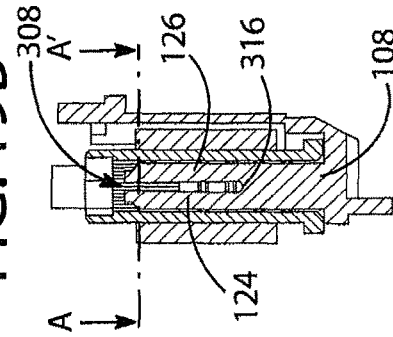


FIG. 19C

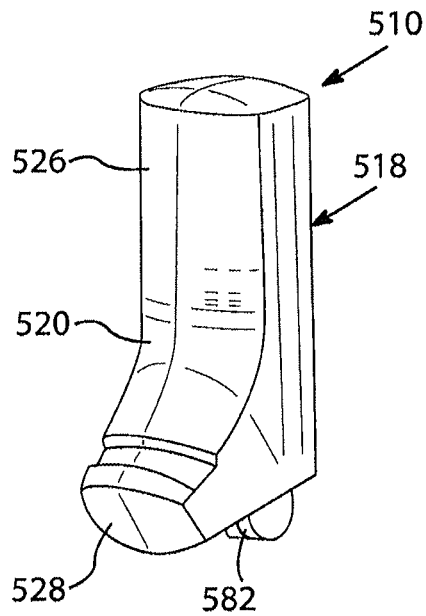


FIG. 21

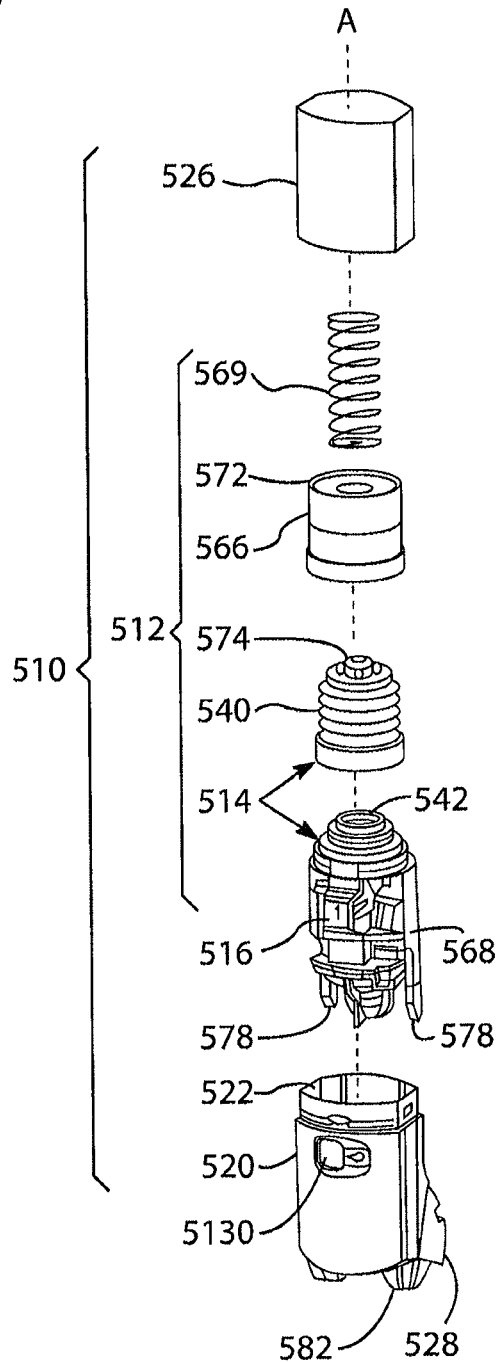


FIG. 22

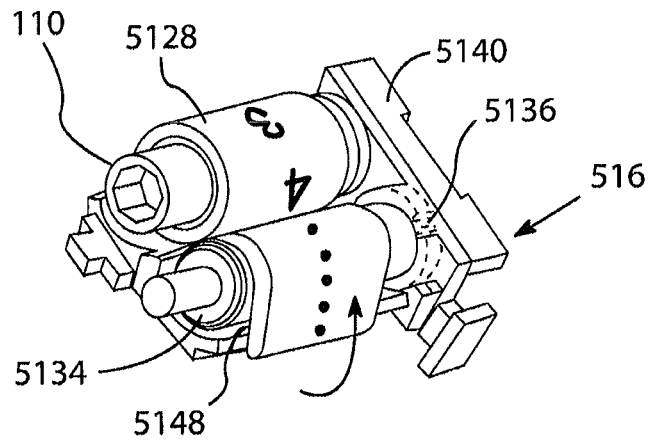


FIG. 23

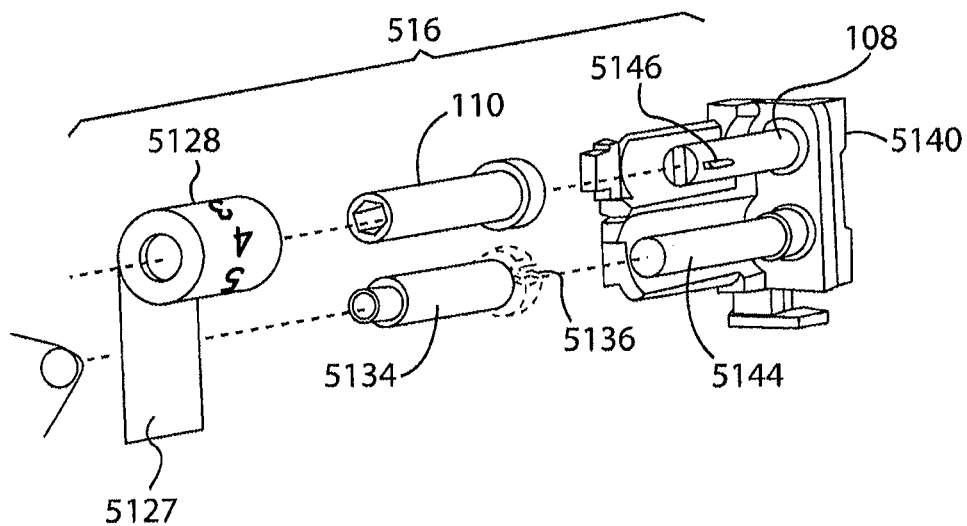


FIG. 24

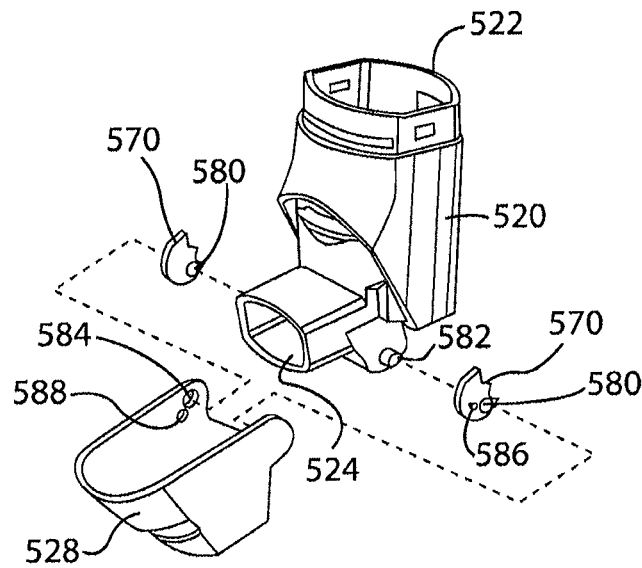


FIG. 25

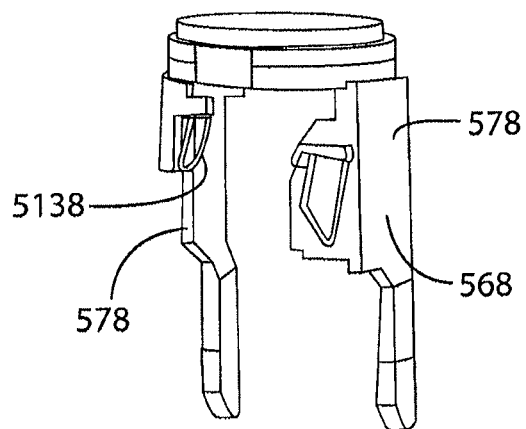


FIG. 26

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DOSE COUNTER FOR INHALER HAVING AN ANTI-REVERSE ROTATION ACTUATOR

CROSS-REFERENCE TO RELATED APPLICATIONS

This patent application is a continuation patent application of U.S. Non-Provisional patent application Ser. No. 14/699,584, filed Apr. 29, 2015, which is a continuation patent application of U.S. Non-Provisional patent application Ser. No. 14/103,353, filed Dec. 11, 2013, which is a divisional patent application of U.S. Non-Provisional patent application Ser. No. 13/110,532, filed May 18, 2011, now U.S. Pat. No. 8,978,966, issued Mar. 17, 2015, which claims priority to U.S. Provisional Patent Application No. 61/345,763, filed May 18, 2010, and U.S. Provisional Patent Application No. 61/417,659, filed Nov. 29, 2010, each of which is incorporated herein by reference in its entirety for any and all purposes.

FIELD OF THE INVENTION

The present invention relates to dose counters for inhalers, inhalers and methods of assembly thereof. The invention is particularly applicable to metered dose inhalers including dry power medicament inhalers, breath actuated inhalers and manually operated metered dose medicament inhalers.

BACKGROUND OF THE INVENTION

Metered dose inhalers can comprise a medicament-containing pressurised canister containing a mixture of active drug and propellant. Such canisters are usually formed from a deep-drawn aluminium cup having a crimped lid which carries a metering valve assembly. The metering valve assembly is provided with a protruding valve stem which, in use is inserted as a push fit into a stem block in an actuator body of an inhaler having a drug delivery outlet. In order to actuate a manually operable inhaler, the user applies by hand a compressive force to a closed end of the canister and the internal components of the metering valve assembly are spring loaded so that a compressive force of approximately 15 to 30N is required to activate the device in some typical circumstances.

In response to this compressive force the canister moves axially with respect to the valve stem and the axial movement is sufficient to actuate the metering valve and cause a metered quantity of the drug and the propellant to be expelled through the valve stem. This is then released into a mouthpiece of the inhaler via a nozzle in the stem block, such that a user inhaling through the outlet of the inhaler will receive a dose of the drug.

A drawback of self-administration from an inhaler is that it is difficult to determine how much active drug and/or propellant are left in the inhaler, if any, especially of the active drug and this is potentially hazardous for the user since dosing becomes unreliable and backup devices not always available.

Inhalers incorporating dose counters have therefore become known.

WO 98/028033 discloses an inhaler having a ratchet mechanism for driving a tape drive dose counter. A shaft onto which tape is wound has a friction clutch or spring for restraining the shaft against reverse rotation.

EP-A-1486227 discloses an inhaler for dry powered medicament having a ratchet mechanism for a tape dose counter which is operated when a mouthpiece of the inhaler

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is closed. Due to the way in which the mouthpiece is opened and closed, and actuation pawl of the device which is mounted on a yoke, travels a known long stroke of consistent length as the mouthpiece is opened and closed.

WO 2008/119552 discloses a metered-dose inhaler which is suitable for breath-operated applications and operates with a known and constant canister stroke length of 3.04 mm+/-0.255 mm. A stock bobbin of the counter, from which a tape is unwound, rotates on a shaft having a split pin intended to hold the stock bobbin taut. However, some dose counters do not keep a particularly reliable count, such as if they are dropped onto a hard surface.

More recently, it has become desirable to improve dose counters further and, in particular, it is felt that it would be useful to provide extremely accurate dose counters for manually-operated canister-type metered dose inhalers. Unfortunately, in these inhalers, it has been found in the course of making the present invention that the stroke length of the canister is to a very large extent controlled on each dose operation by the user, and by hand. Therefore, the stroke length is highly variable and it is found to be extremely difficult to provide a highly reliable dose counter for these applications. The dose counter must not count a dose when the canister has not fired since this might wrongly indicate to the user that a dose has been applied and if done repeatedly the user would throw away the canister or whole device before it is really time to change the device due to the active drug and propellant reaching a set minimum. Additionally, the canister must not fire without the dose counter counting because the user may then apply another dose thinking that the canister has not fired, and if this is done repeatedly the active drug and/or propellant may run out while the user thinks the device is still suitable for use according to the counter. It has also been found to be fairly difficult to assembly some known inhaler devices and the dose counters therefor. Additionally, it is felt desirable to improve upon inhalers by making them easily usable after they have been washed with water.

The present invention aims to alleviate at least to a certain extent one or more of the problems of the prior art.

SUMMARY OF THE INVENTION

According to a first aspect of the present invention there is provided a dose counter for an inhaler, the dose counter having a counter display arranged to indicate dosage information, a drive system arranged to move the counter display incrementally in a first direction from a first station to a second station in response to actuation input, wherein a regulator is provided which is arranged to act upon the counter display at the first station to regulate motion of the counter display at the first station to incremental movements.

The regulator is advantageous in that it helps prevent unwanted motion of the counter display if the counter is dropped.

According to a further aspect of the present invention, the regulator provides a resistance force of greater than 0.1 N against movement of the counter display. According to still a further aspect of the present invention, the resistance force is greater than 0.3 N. According to yet a further aspect of the present invention, the resistance force is from 0.3 to 0.4 N.

Preferably, the counter comprises a tape.

Preferably, the tape has dose counter indicia displayed thereon. The first station may comprise a region of the dose counter where tape is held which is located before a display location, such as a display window, for the counter indicia.

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The first station may comprise a first shaft, the tape being arranged on the first shaft and to unwind therefrom upon movement of the counter display.

The first shaft may be mounted for rotation relative to a substantially rotationally fixed element of the dose counter.

The regulator may comprise at least one projection which is arranged on one of the first shaft and the substantially rotationally fixed element and to engage incrementally with one or more formations on the other of the first shaft and the substantially rotationally fixed element.

At least two said projections may be provided. Exactly two said projections may be provided.

Each projection may comprise a radiused surface.

The at least one projection may be located on the substantially fixed element which may comprise a fixed shaft which is fixed to a main body of the dose counter, the first shaft being rotationally mounted to the fixed shaft.

Preferably, the fixed shaft has at least two resiliently flexible legs (or forks). Each leg may have at least one said projection formed in an outwardly facing direction thereon, said one or more formations being formed on an inwardly facing engagement surface of the first shaft, said at least one projection being arranged to resiliently engage said one or more formations. Preferably, a series of said formations are provided. An even number of said formations may be provided. Eight to twelve of said formations may be provided. In one embodiment, ten said formations are provided.

Each said formation may comprise a concavity formed on an engagement surface. Each concavity may comprise a radiused surface wall portion which preferably merges on at least one side thereof into a flat wall portion surface. The engagement surface may include a series of said concavities, and convex wall portions of the engagement surface may be formed between each adjacent two said concavities, each said convex wall portion comprising a convex radiused wall portion.

Each convex radiused wall portion of each convex wall portion may be connected by said flat wall portion surfaces to each adjacent concavity.

The fixed shaft may comprise a split pin with fork legs and each projection may be located on a said fork leg.

The first shaft may comprise a substantially hollow bobbin.

Said at least one formation may be located on an inner surface of the bobbin. In other embodiments it may be located on an outer surface thereof. Said engagement surface may extend partially along said bobbin, a remainder of the respective inner or outer surface having a generally smooth journal portion along at least a portion thereof.

The drive system may comprise a tooth ratchet wheel arranged to act upon a second shaft which is located at the second station, the second shaft being rotatable to wind the tape onto the second shaft.

The second shaft may be located on a main body of the dose counter spaced from and parallel to the first shaft.

The ratchet wheel may be fixed to the second shaft is arranged to rotate therewith. The ratchet wheel may be secured to an end of the second shaft and aligned coaxially with the second shaft.

The dose counter may include anti-back drive system which is arranged to restrict motion of the second shaft. The anti-back drive system may include a substantially fixed tooth arranged to act upon teeth of the ratchet wheel.

According to a further aspect of the present invention, a dose counter includes an anti-back drive system which is arranged to restrict motion of the second shaft in a tape winding direction.

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According to a further aspect of the present invention there is provided a shaft for holding counter tape in a dose counter for an inhaler, the shaft having an engagement surface including incrementally spaced formations located around a periphery thereof, the formations comprising a series of curved concavities and convex portions.

The shaft may comprise a hollow bobbin.

The engagement surface may be a generally cylindrical inwardly directed surface.

The engagement surface may include a flat surface wall portion joining each concavity and convex wall portion.

Each concavity may comprise a radiused wall portion.

Each convex wall portion may comprise a radiused wall portion.

Said concavities may be regularly spaced around a longitudinal axis of the shaft.

Said convex wall portions may be regularly spaced around a longitudinal axis of the shaft.

In some embodiments there may be from eight to twelve said concavities and/or convex wall portions regularly spaced around a longitudinal axis thereof.

One embodiment includes ten said concavities and/or convex wall portions regularly spaced around a longitudinal axis of the shaft.

According to a further aspect of the present invention there is provided a shaft and counter tape assembly for use in a dose counter for an inhaler, the assembly comprising a rotatable shaft and a counter tape which is wound around the shaft and is adapted to unwind therefrom upon inhaler actuation, the shaft having an engagement surface which includes incrementally spaced formations located around a periphery thereof.

According to a further aspect of the present invention there is provided an inhaler for the inhalation of medication and the like, the inhaler including a dose counter as in the first aspect of the present invention.

A preferred construction consists of a manually operated metered dose inhaler including a dose counter chamber including a dose display tape driven by a ratchet wheel which is driven in turn by an actuator pawl actuated by movement of a canister, the tape unwinding from a stock bobbin during use of the inhaler, a rotation regulator being provided for the stock bobbin and comprising a wavelike engagement surface with concavities which engage against control elements in the form of protrusions on resilient forks of a split pin thereby permitting incremental unwinding of the stock bobbin yet resisting excessive rotation if the inhaler is dropped onto a hard surface.

According to another aspect of the present invention there is provided a dose counter for a metered dose inhaler having a body arranged to retain a medicament canister of predetermined configuration for movement of the canister relative thereto; the dose counter comprising: an incremental counting system for counting doses, the incremental counting system having a main body, an actuator arranged to be driven in response to canister motion and to drive an incremental output member in response to canister motion, the actuator and incremental output member being configured to have predetermined canister fire and count configurations in a canister fire sequence, the canister fire configuration being determined by a position of the actuator relative to a datum at which the canister fires medicament and the count configuration being determined by a position of the actuator relative to the datum at which the incremental count system makes an incremental count, wherein the actuator is

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arranged to reach a position thereof in the count configuration at or after a position thereof in the canister fire configuration.

This arrangement has been found to be highly advantageous since it provides an extremely accurate dose counter which is suitable for use with manually operated metered dose inhalers. It has been found that dose counters with these features have a failure rate of less than 50 failed counts per million full canister activation depressions. It has been found in the course of making the present invention that highly reliable counting can be achieved with the dose counter counting at or soon after the point at which the canister fires. It has been is covered by the present inventors that momentum and motion involved in firing the canister, and in some embodiments a slight reduction in canister back pressure on the user at the time of canister firing, can very reliably result in additional further motion past the count point.

The actuator and incremental counting system may be arranged such that the actuator is displaced less than 1 mm, typically 0.25 to 0.75 mm, more preferably about 0.4 to 0.6 mm, relative to the body between its location in the count and fire configurations, about 0.48 mm being preferred. The canister, which can move substantially in line with the actuator, can reliably move this additional distance so as to achieve very reliable counting.

The incremental count system may comprise a ratchet mechanism and the incremental output member may comprise a ratchet wheel having a plurality of circumferentially spaced teeth arranged to engage the actuator.

The actuator may comprise an actuator pawl arranged to engage on teeth of the ratchet wheel. The actuator pawl may be arranged to be connected to or integral with an actuator pin arranged to engage and be depressed by a medicament canister bottom flange. The actuator pawl may be generally U-shaped having two parallel arms arranged to pull on a central pawl member arranged substantially perpendicular thereto. This provides a very reliable actuator pawl which can reliably pull on the teeth of the ratchet wheel.

The incremental count system may include a tape counter having tape with incremental dose indicia located thereon, the tape being positioned on a tape stock bobbin and being arranged to unwind therefrom.

The actuator and incremental output member may be arranged to provide a start configuration at which the actuator is spaced from the ratchet output member, a reset configuration at which the actuator is brought into engagement with the incremental output member during a canister fire sequence, and an end configuration at which the actuator disengages from the ratchet output during a canister fire sequence.

The actuator may be arranged to be located about 1.5 to 2.0 mm, from its location in the fire configuration, when in the start configuration, about 1.80 mm being preferred.

The actuator may be arranged to be located about 1.0 to 1.2 mm, from its location in the fire configuration, when in the reset configuration, about 1.11 mm being preferred.

The actuator may be arranged to be located about 1.1 to 1.3 mm, from its location in the fire configuration, when in the end configuration, about 1.18 mm being preferred.

These arrangements provide extremely reliable dose counting, especially with manually operated canister type metered dose inhalers.

The main body may include a formation for forcing the actuator to disengage from the incremental output member when the actuator is moved past the end configuration. The formation may comprise a bumped up portion of an other-

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wise generally straight surface against which the actuator engages and along which it is arranged to slide during a canister firing sequence.

The dose counter may include a counter pawl, the counter pawl having a tooth arranged to engage the incremental output member, the tooth and incremental output member being arranged to permit one way only incremental relative motion therebetween. When the incremental output member comprises a ratchet wheel, the tooth can therefore serve as an anti-back drive tooth for the ratchet wheel, thereby permitting only one way motion or rotation thereof.

The counter pawl may be substantially fixedly mounted on the main body of the incremental count system and the counter pawl may be arranged to be capable of repeatedly engaging equi-spaced teeth of the incremental output member in anti-back drive interlock configurations as the counter is operated. The counter pawl may be positioned so that the incremental output member is halfway, or substantially halfway moved from one anti-back drive interlock configuration to the next when the actuator and incremental output member are in the end configuration thereof. This is highly advantageous in that it minimises the risk of double counting or non-counting by the dose counter.

According to a further aspect of the invention there is provided an inhaler comprising a main body arranged to retain a medicament canister of predetermined configuration and a dose counter mounted in the main body.

The inhaler main body may include a canister receiving portion and a separate counter chamber, the dose counter being located within the main body thereof, the incremental output member and actuator thereof inside the counter chamber, the main body of the inhaler having wall surfaces separating the canister-receiving portion and the counter chamber, the wall surfaces being provided with a communication aperture, an actuation member extending through the communication aperture to transmit canister motion to the actuator.

According to a further aspect of the present invention there is a provided an inhaler for metered dose inhalation, the inhaler comprising a main body having a canister housing arranged to retain a medicament canister for motion therein, and a dose counter, the dose counter having an actuation member having at least a portion thereof located in the canister housing for operation by movement of a medicament canister, wherein the canister housing has an inner wall, and a first inner wall canister support formation located directly adjacent the actuation member.

This is highly advantageous in that the first inner wall canister support formation can prevent a canister from rocking too much relative to the main body of the inhaler. Since the canister may operate the actuation member of the dose counter, this substantially improves dose counting and avoids counter errors.

The canister housing may have a longitudinal axis which passes through a central outlet port thereof, the central outlet port being arranged to mate with an outer canister fire stem of a medicament canister, the inner wall canister support formation, the actuation member and the outlet port lying in a common plane coincident with the longitudinal axis. Accordingly, this construction may prevent the canister from rocking towards the position of the dose counter actuation member, thereby minimising errors in counting.

The canister housing may have a further inner canister wall support formation located on the inner wall opposite, or substantially opposite, the actuation member. Accordingly, the canister may be supported against rocking motion away from the actuator member so as to minimise count errors.

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The canister housing may be generally straight and tubular and may have an arrangement in which each said inner wall support formation comprises a rail extending longitudinally along the inner wall.

Each said rail may be stepped, in that it may have a first portion located towards a medicine outlet end or stem block of the canister housing which extends inwardly a first distance from a main surface of the inner wall and a second portion located toward an opposite end of the canister chamber which extends inwardly a second, smaller distance from the main surface of the inner wall. This may therefore enable easy insertion of a canister into the canister housing such that a canister can be lined up gradually in step wise function as it is inserted into the canister housing.

The inhaler may include additional canister support rails which are spaced around an inner periphery of the inner wall of the canister housing and which extend longitudinally therealong.

At least one of the additional rails may extend a constant distance inwardly from the main surface of the inner wall.

At least one of the additional rails may be formed with a similar configuration to the first inner wall canister support formation.

The dose counter may, apart from said at least a portion of the actuation member, be located in a counter chamber separate from the canister housing, the actuation member comprising a pin extending through an aperture in a wall which separates the counter chamber and the canister housing.

According to a further aspect of the present invention there is provided an inhaler for inhaling medicaments having: a body for retaining a medicament store; the body including a dose counter, the dose counter having a moveable actuator and a return spring for the actuator, the return spring having a generally cylindrical and annular end; the body having a support formation therein for supporting said end of the return spring, the support formation comprising a shelf onto which said end is engageable and a recess below the shelf.

This shelf and recess arrangement is highly advantageous since it allows a tool (such as manual or mechanical tweezers) to be used to place the return spring of the actuator onto the shelf with the tool then being withdrawn at least partially via the recess.

The shelf may be U-shaped.

The support formation may include a U-shaped upstanding wall extending around the U-shaped shelf, the shelf and upstanding wall thereby forming a step and riser of a stepped arrangement.

The recess below the shelf may also be U-shaped.

At least one chamfered surface may be provided at an entrance to the shelf. This may assist in inserting the actuator and return spring into position.

A further aspect of the invention provides a method of assembly of an inhaler which includes the step of locating said end of said spring on the shelf with an assembly tool and then withdrawing the assembly tool at least partly via the recess. This assembly method is highly advantageous compared to prior art methods in which spring insertion has been difficult and in which withdrawal of the tool has sometimes accidentally withdrawn the spring again.

The cylindrical and annular end of the spring may be movable in a direction transverse to its cylindrical extent into the shelf while being located thereon.

According to a further aspect of the present invention there is provided an inhaler for inhaling medicament, the inhaler having a body for retaining a medicament store; and

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a dose counter, the dose counter having a moveable actuator and a chassis mounted on the body; the chassis being heat staked in position on the body. This is highly advantageous in that the chassis can be very accurately positioned and held firmly in place, thereby further improving counting accuracy compared to prior art arrangements in which some movement of the chassis relative to the body may be tolerated in snap-fit connections.

The chassis may have at least one of a pin or aperture heat staked to a respective aperture or pin of the body.

The chassis may have a ratchet counter output member mounted thereon.

The ratchet counter output member may comprise a ratchet wheel arranged to reel in incrementally a dose meter tape having a dosage indicia located thereon.

According to a further aspect of the present invention there is provided a method of assembling an inhaler including the step of heat staking the chassis onto the body. The step of heat staking is highly advantageous in fixedly positioning the chassis onto the body in order to achieve highly accurate dose counting in the assembled inhaler.

The method of assembly may include mounting a spring-returned ratchet actuator in the body before heat staking the chassis in place. The method of assembly may include pre-assembling the chassis with a dose meter tape prior to the step of heat staking the chassis in place. The method of assembly may include attaching a dose meter cover onto the body after the heat staking step. The cover may be welded onto the body or may in some embodiments be glued or otherwise attached in place.

According to a further aspect of the present invention there is provided an inhaler for inhaling medicament and having a body, the body have a main part thereof for retaining a medicament store; and a dose counter, the dose counter being located in a dose counter chamber of the body which is separated from the main part of the body, the dose counter chamber of the body having a dosage display and being perforated so as to permit the evaporation of water or aqueous matter in the dose counter chamber into the atmosphere.

This is highly advantageous since it enables the inhaler to be thoroughly washed and the dose counting chamber can thereafter dry out fully.

The display may comprise a mechanical counter display inside the dose counter chamber and a window for viewing the mechanical counter display. The mechanical counter display may comprise a tape. The perforated dose counter chamber may therefore enable reliable washing of the inhaler, if desired by the user, and may therefore dry out without the display window misting up.

The dose counter chamber may be perforated by a drain hole formed through an outer hole of the body. The drain hole may be located at a bottom portion of the body of the inhaler, thereby enabling full draining of the inhaler to be encouraged after washing when the inhaler is brought into an upright position.

According to a further aspect of the present invention there is provided a dose counter for an inhaler, the dose counter having a display tape arranged to be incrementally driven from a tape stock bobbin onto an incremental tape take-up drive shaft, the bobbin having an internal bore supported by and for rotation about a support shaft, at least one of the bore and support shaft having a protrusion which is resiliently biased into frictional engagement with the other of the bore and support shaft with longitudinally extending mutual frictional interaction. This arrangement may provide good friction for the bobbin, thereby improving tape counter

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display accuracy and preventing the bobbin from unwinding undesirably for example if the inhaler is accidentally dropped.

The support shaft may be forked and resilient for resiliently biasing the support shaft and bore into frictional engagement.

The support shaft may have two forks, or more in some cases, each having a radially extending protrusion having a friction edge extending therealong parallel to a longitudinal axis of the support shaft for frictionally engaging the bore of the support shaft with longitudinally extending frictional interaction therebetween.

The bore may be a smooth circularly cylindrical or substantially cylindrical bore.

Each of the above inhalers in accordance with aspects of the present invention may have a medicament canister mounted thereto.

The canister may comprise a pressurised metered dose canister having a reciprocally movable stem extending therefrom and movable into a main canister portion thereof for releasing a metered dose of medicament under pressure, for example by operating a metered dose valve inside the canister body. The canister may be operable by pressing by hand on the main canister body.

In cases in which one or more support rails or inner wall support formations are provided, the canister may at all times when within the canister chamber have a clearance of about 0.25 to 0.35 mm from the first inner wall support formation. The clearance may be almost exactly 0.3 mm. This clearance which may apply to the canister body itself or to the canister once a label has been applied, is enough to allow smooth motion of the canister in the inhaler while at the same time preventing substantial rocking of the canister which could result in inaccurate counting by a dose counter of the inhaler, especially when lower face of the canister is arranged to engage an actuator member of the dose counter for counting purposes.

According to a further aspect of the invention, a method of assembling a dose counter for an inhaler comprises the steps of providing a tape with dosing indicia thereon; providing tape positioning indicia on the tape; and stowing the tape while monitoring for the tape positioning indicia with a sensor. The method advantageously permits efficient and accurate stowing of the tape, e.g. by winding.

The dosing indicia may be provided as numbers, the tape positioning indicia may be provided as one or more lines across the tape. The stowing step comprises winding the tape onto a bobbin or shaft, and, optionally, stopping winding when the positioning indicia are in a predetermined position. The tape may be provided with pixelated indicia at a position spaced along the tape from the positioning indicia. The tape may also be provided with a priming dot.

According to a further aspect of the invention, a tape system for a dose counter for an inhaler has a main elongate tape structure, and dosing indicia and tape positioning indicia located on the tape structure. The tape positioning indicia may comprise at least one line extending across the tape structure. The tape system may comprise pixelated indicia located on the tape structure and spaced from the positioning indicia. The tape system may comprise a priming dot located on the tape structure. The positioning indicia may be located between the timing dot and the pixelated indicia. The main elongate tape structure may have at least one end thereof wound on a bobbin or shaft.

A further aspect of the invention provides a method of designing an incremental dose counter for an inhaler comprising the steps of calculating nominal canister fire and

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dose counter positions for a dose counter actuator of the inhaler; calculating a failure/success rate for dose counters built to tolerance levels for counting each fire of inhalers in which the dose counter actuators may be applied; and selecting a tolerance level to result in said failure/success rate to be at or below/above a predetermined value. This is highly advantageous in that it allows an efficient and accurate prediction of the reliability of a series of inhaler counters made in accordance with the design.

The method of designing may include selecting the failure/success rate as a failure rate of no more than one in 50 million. The method of designing may include setting an average count position for dose counters built to the tolerances to be at or after an average fire position thereof during canister firing motion. The method of designing may include setting the average count position to be about 0.4 to 0.6 mm after the average fire position, such as about 0.48 mm after. The method of designing may include setting tolerances for the standard deviation of the fire position in dose counters built to the tolerances to be about 0.12 to 0.16 mm, such as about 0.141 mm. The method of designing may include setting tolerances for the standard deviation of the count positions in dose counters built to the tolerances to be about 0.07 to 0.09 mm, such as about 0.08 mm. A further aspect of the invention provides a computer implemented method of designing an incremental dose counter for an inhaler which includes the aforementioned method of designing.

A further aspect of the invention provides a method of manufacturing in a production run a series of incremental dose counters for inhalers which comprises manufacturing the series of dose counters in accordance with the aforementioned method of designing.

A further aspect of the invention provides a method of manufacturing a series of incremental dose counters for inhalers, which comprises manufacturing the dose counters with nominal canister fire and dose count positions of a dose counter actuator relative to a dose counter chassis (or inhaler main body), and which includes building the dose counters with the average dose count position in the series being, in canister fire process, at or after the average canister fire position in the series.

According to a further aspect of the invention, the method provides fitting each dose counter in the series of incremental dose counters to a corresponding main body of an inhaler.

These aspects advantageously provide for the production run of a series of inhalers and dose counters which count reliably in operation.

According to a further aspect of the invention, an incremental dose counter for a metered dose inhaler has a body arranged to retain a canister for movement of the canister relative thereto, the incremental dose counter having a main body, an actuator arranged to be driven and to drive an incremental output member in a count direction in response to canister motion, the actuator being configured to restrict motion of the output member in a direction opposite to the count direction. This advantageously enables an inhaler dose counter to keep a reliable count of remaining doses even if dropped or otherwise jolted.

The output member may comprise a ratchet wheel. The actuator may comprise a pawl and in which the ratchet wheel and pawl are arranged to permit only one-way ratcheting motion of the wheel relative to the pawl. The dose counter may include an anti-back drive member fixed to the main body. In a rest position of the dose counter, the ratchet wheel is capable of adopting a configuration in which a back surface of one tooth thereof engages the anti-back drive member and the pawl is spaced from an adjacent back

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surface of another tooth of the ratchet wheel without positive drive/blocking engagement between the pawl and wheel.

BRIEF DESCRIPTION OF THE DRAWINGS

The present invention may be carried out in various ways and preferred embodiment of a dose counter, inhaler and methods of assembly, design and manufacture will now be described with reference to the accompanying drawings in which:

FIG. 1 is an isometric view of a main body of an embodiment of an inhaler related to the invention together with a mouthpiece cap therefor;

FIG. 2 is a top plan view of the components as shown in FIG. 1;

FIG. 3A is a section on the plane 3A-3A in FIG. 2;

FIG. 3B is a view corresponding to FIG. 3A but with a dose counter fitted to the main body of the inhaler;

FIG. 4A is an exploded view of the inhaler main body, mouthpiece cap, dose counter and a dose counter window;

FIG. 4B is a view in the direction 4B in FIG. 4C of a spring retainer of the dose counter;

FIG. 4C is a top view of the spring retainer of FIG. 4B;

FIG. 5 is a bottom view of the assembled inhaler main body, mouthpiece cap, dose counter and dose counter window;

FIGS. 6A, 6B, 6C, 6D, 6E, 6F, 6G and 6H are various views of dose counter components of the inhaler;

FIGS. 7A and 7B are sectional views showing canister clearance inside the main body of the inhaler;

FIG. 7C is a further sectional view similar to that of FIG. 7B but with the canister removed;

FIG. 7D is a top plan view of the inhaler main body;

FIGS. 8A, 8B, 8C and 8D show the inhaler main body and dose counter components during assembly thereof;

FIG. 9 shows a sectional side view of a datum line for an actuator pawl of the dose counter;

FIGS. 10A, 10B, 10C, 10D, 10E and 10F show various side views of positions and configurations of the actuator pawl, a ratchet wheel, and a count pawl;

FIG. 11 shows distributions for tolerances of start, reset, fire, count and end positions for the actuator of the dose counter;

FIG. 12 is an enlarged version of part of FIG. 4A;

FIG. 13 shows an end portion of a tape of the dose counter;

FIG. 14 shows a computer system for designing the dose counter;

FIG. 15 is an isometric view of a stock bobbin modified in accordance with the present invention for use in the dose counter of the inhaler of FIGS. 1 to 14;

FIG. 16 shows an end view of the stock bobbin of FIG. 15;

FIG. 17 is a section through a longitudinal axis of the stock bobbin of FIGS. 15 and 16;

FIGS. 18A, 18B and 18C are views of the stock bobbin of FIGS. 15 to 17 mounted in the dose counter chassis of FIGS. 1 to 14, with the control elements of the forks of the second shaft (or split pin) having a profile slightly different to that in FIG. 6F, with the forks in a compressed configuration;

FIGS. 19A, 19B and 19C are views equivalent to FIGS. 18A to 18C but with the forks in a more expanded configuration due to a different rotational position of the stock bobbin;

FIG. 20 is an isometric view of the chassis assembled and including the stock bobbin of FIGS. 15 to 17 but excluding the tape for reasons of clarity;

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FIG. 21 is a view of a preferred embodiment of a dry powder inhaler in accordance with the present invention;

FIG. 22 is an exploded view of the inhaler of FIG. 21;

FIG. 23 is a view of a dose counter of the inhaler of FIG. 21;

FIG. 24 is an exploded view of the dose counter shown in FIG. 23;

FIG. 25 is an exploded view of parts of the inhaler of FIG. 21; and

FIG. 26 is a view of a yoke of the inhaler of FIG. 21.

DETAILED DESCRIPTION OF THE INVENTION

FIG. 1 shows a main body 10 of a manually operated metered dose inhaler 12 in accordance with an embodiment related to the present invention and having a mouthpiece cap 14 securable over a mouthpiece 16 of the main body.

The main body has a canister chamber 18 into which a canister 20 (FIG. 7A) is slideable. The canister 20 has a generally cylindrical main side wall 24, joined by a tapered section 26 to a head portion 28 having a substantially flat lower face 30 which has an outer annular drive surface 32 arranged to engage upon and drive an actuation pin 34 of a dose counter 36 as will be described. Extending centrally and axially from the lower face 30 is a valve stem 38 which is arranged to sealingly engage in a valve stem block 40 of the main body 10 of the inhaler 12. The valve stem block 40 has a passageway 42 leading to a nozzle 44 for directing the contents of the canister 20, namely active drug and propellant, towards an air outlet 46 of the inhaler main body 12. It will be appreciated that due to gaps 48 between the canister 20 and an inner wall 50 of the main body 10 of the inhaler 12 an open top 52 of the main body 10 forms an air inlet into the inhaler 12 communicating via air passageway 54 with the air outlet 46, such that canister contents exiting nozzle 44 mix with air being sucked by the user through the air passageway 54 in order to pass together through the air outlet and into the mouth of the user (not shown).

The dose counter 36 will now be described. The dose counter 36 includes an actuation pin 34 biased upwardly from underneath by a return spring 56 once installed in the main body 10. As best shown in FIGS. 4A, 6H and 8A, the pin 34 has side surfaces 58, 60 arranged to slide between corresponding guide surfaces 62, 64 located in a dose counter chamber 66 of the main body 10, as well as an end stop surface 68 arranged to engage a corresponding end stop 70 formed in the dose counter chamber 66 to limit upward movement of the pin 34. The pin 34 has a top part 72 which is circularly cylindrical and extends through an aperture 74 formed through a separator wall 76 which separates the canister chamber 18 from the dose counter chamber 66. The top part 72 of the pin 34 has a flat top surface 78 which is arranged to engage the outer annular drive surface 32 of the canister 20.

The actuation pin 34 is integrally formed with a drive or actuator pawl 80. The actuator pawl 80 has a generally inverted U-shape configuration, having two mutually spaced and parallel arms 82, 84 extending from a base portion of the actuation pin 34, each holding at respective distal ends 88 thereof opposite ends of a pawl tooth member 90 which extends in a direction substantially perpendicular to the arms 82, 84, so as to provide what may be considered a "saddle" drive for pulling on each of the 11 drive teeth 92 of a ratchet wheel 94 of an incremental drive system 96 or ratchet mechanism 96 of the dose counter 36. As shown for example in FIG. 10B, the pawl tooth member 90 has a sharp lower

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longitudinal side edge 98 arranged to engage the drive teeth 92, the edge-to-surface contact provided by this engagement providing very accurate positioning of the actuator pawl 80 and resultant rotational positioning of the ratchet wheel 94.

The dose counter 36 also has a chassis preassembly 100 which, as shown in FIGS. 4A and 6A, includes a chassis 102 having a first shaft 104 receiving the ratchet wheel 94 which is secured to a tape reel shaft 106, and a second shaft (or split pin) 108 which is parallel to and spaced from the first shaft 104 and which slidably and rotationally receives a tape stock bobbin 110.

As shown in FIG. 6B, when the inhaler has not been used at all, the majority of a tape 112 is wound on the tape stock bobbin 110 and the tape 112 has a series of regularly spaced numbers 114 displayed therealong to indicate a number of remaining doses in the canister 20. As the inhaler is repeatedly used, the ratchet wheel 94 is rotated by the actuator pawl 80 due to operation of the actuation pin 34 by the canister 20 and the tape 112 is incrementally and gradually wound on to the tape reel shaft 106 from the second shaft 108. The tape 112 passes around a tape guide 116 of the chassis 102 enabling the numbers 114 to be displayed via a window 118 in a dose counter chamber cover 120 having a dose marker 132 formed or otherwise located thereon.

As shown in FIGS. 6A and 6D, the second shaft 108 is forked with two forks 124, 126. The forks 124, 126 are biased away from one another. The forks have located thereon at diametrically opposed positions on the second shaft 108 friction or control elements 128, 130, one on each fork. Each control element extends longitudinally along its respective fork 124, 126 and has a longitudinally extending friction surface 132, 134 which extends substantially parallel to a longitudinal axis of the second shaft and is adapted to engage inside a substantially cylindrical bore 136 inside the tape stock bobbin 110. This control arrangement provided between the bore 136 and the control elements 128, 130 provides good rotational control for the tape stock bobbin 110 such that it does not unwind undesirably such as when the inhaler is dropped. The tape force required to unwind the tape stock bobbin 110 and overcome this friction force is approximately 0.1 N.

As can be seen in FIG. 6D, as well as FIGS. 6G and 10A to 10F, the chassis 102 is provided with an anti-back drive tooth 138 or count pawl 138 which is resiliently and substantially fixedly mounted thereto. As will be described below and as can be seen in FIGS. 10A to 10F, when the actuation pin 34 is depressed fully so as to fire the metered valve (not shown) inside the canister 20, the actuator pawl 80 pulls down on one of the teeth 92 of the ratchet wheel 94 and rotates the wheel 94 anticlockwise as shown in FIG. 6D so as to jump one tooth 92 past the count pawl 138, thereby winding the tape 112 a distance incrementally relative to the dose marker 122 on the dose counter chamber 120 so as to indicate that one dose has been used.

With reference to FIG. 10B, the teeth of the ratchet wheel 94 have tips 143 which are radiused with a 0.1 mm radius between the flat surfaces 140, 142. The ratchet wheel 94 has a central axis 145 which is 0.11 mm above datum plane 220 (FIG. 9). A top/nose surface 147 of the anti-back drive tooth 138 is located 0.36 mm above the datum plane 220. The distance vertically (i.e. transverse to datum plane 220—FIG. 9) between the top nose surface 147 of the anti-back drive tooth is 0.25 mm from the central axis 145 of the wheel 94. Bump surface 144 has a lateral extent of 0.20 mm, with a vertical length of a flat 145' thereof being 1 mm, the width of the bump surface being 1.22 mm (in the direction of the axis 145), the top 149 of the bump surface 144 being 3.02

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mm vertically below the axis 145, and the flat 145' being spaced a distance sideways (i.e. parallel to the datum plane 220) 2.48 mm from the axis 145. The top surface 78 of the pin 34 (FIG. 6H) is 11.20 mm above the datum plane 220 (FIG. 9) when the actuator pawl 80 and pin 34 are in the start configuration. The length of the valve stem 22 is 11.39 mm and the drive surface 32 of the canister 20 is 11.39 mm above the datum plane 220 when the canister is at rest waiting to be actuated, such that there is a clearance of 0.19 mm between the canister 20 and the pin 34 in this configuration.

FIGS. 10A and 10B show the actuator pawl 80 and ratchet wheel 94 and count pawl 138 in a start position in which the flat top 78 of the pin 34 has not yet been engaged by the outer annular drive surface 32 of the canister 20 or at least has not been pushed down during a canister depression.

In this "start" position, the count pawl 138 engages on a non-return back surface 140 of one of the teeth 92 of the ratchet wheel 94. The lower side edge 98 of the actuator pawl is a distance "D" (FIG. 9) 1.33 mm above datum plane 220 which passes through bottom surface or shoulder 41 of valve stem block 40, the datum plane 220 being perpendicular to a main axis "X" of the main body 10 of the inhaler 12 which is coaxial with the centre of the valve stem block bore 43 and parallel to a direction of sliding of the canister 20 in the main body 10 of the inhaler 12 when the canister is fired.

As shown in FIG. 10B, an advantageous feature of the construction is that the pawl tooth/actuator 90 acts as a supplementary anti-back drive member when the inhaler 12 is not being used for inhalation. In particular, if the inhaler 12 is accidentally dropped, resulting in a jolt to the dose counter 36 then, if the wheel 94 would try to rotate clockwise (backwards) as shown in FIG. 10B, the back surface 140 of a tooth will engage and be blocked by the tooth member 90 of the pawl 80. Therefore, even if the anti-back drive tooth 138 is temporarily bent or overcome by such a jolt, undesirable backwards rotation of the wheel 94 is prevented and, upon the next canister firing sequence, the pawl 90 will force the wheel 94 to catch up to its correct position so that the dose counter 36 continues to provide correct dosage indication.

FIG. 10C shows a configuration in which the actuator pawl 80 has been depressed with the pin 34 by the canister 20 to a position in which the side edge 98 of the pawl tooth member 90 is just engaged with one of the teeth 92 and will therefore upon any further depression of the pin 34 begin to rotate the wheel 94. This is referred to as a "Reset" position or configuration. In this configuration, the lower side edge 98 of the actuator 80 is 0.64 mm above the datum plane 220.

FIG. 10D shows a configuration in which the actuator pawl 80 has been moved to a position lower than that shown in FIG. 10C and in which the metered dose valve (not shown) inside the canister has at this very position fired in order to eject active drug and propellant through the nozzle 44. It will be noted that in this configuration the count pawl 138 is very slightly spaced from the back surface 140 of the same tooth 92 that it was engaging in the configuration of FIG. 10D. The configuration shown in FIG. 10D is known as a "Fire" configuration. In this configuration the lower side edge 98 of the actuator 80 is 0.47 mm below the datum plane 220.

FIG. 10E shows a further step in the sequence, called a "Count" position in which the actuator pawl 80 has rotated the ratchet wheel 94 by the distance circumferentially angularly between two of the teeth 92, such that the count pawl 138 has just finished riding along a forward surface 142 of one of the teeth 92 and has resiliently jumped over the tooth

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into engagement with the back surface **140** of the next tooth. Accordingly, in this "Count" configuration, a sufficiently long stroke movement of the pin **34** has occurred that the tape **112** of the dose counter **36** will just have counted down one dose. In this configuration, the lower side edge **98** of the actuator is 0.95 mm below the datum plane **220**. Accordingly, in this position, the actuator **80** generally, including edge **98**, is 0.48 mm lower than in the fire configuration. It has been found that, although the count configuration happens further on than the fire configuration, counting is highly reliable, with less than 50 failed counts per million. This is at least partially due to momentum effects and to the canister releasing some back pressure on the user in some embodiments as its internal metering valve fires.

In the configuration of FIG. **10F**, the pawl **80** has been further depressed with the pin **34** by the canister **20** to a position in which it is just disengaging from one of the teeth **92** and the actuator pawl **80** is assisted in this disengagement by engagement of one of the arms **84** with a bump surface **144** on the chassis **102** (see FIG. **6G**) and it will be seen at this point of disengagement, which is called an "End" configuration, the count pawl **138** is positioned exactly halfway or substantially halfway between two of the drive teeth **92**. This advantageously means therefore that there is a minimum chance of any double counting or non-counting, which would be undesirable. In the end configuration, the side edge **98** of the actuator is 1.65 mm below the datum plane **220**. It will be appreciated that any further depression of the actuator pawl **80** and pin **34** past the "End" configuration shown in FIG. **10F** will have no effect on the position of the tape **112** displayed by the dose counter **36** since the actuator pawl **80** is disengaged from the ratchet wheel **94** when it is below the position shown in FIG. **10F**.

As shown in FIGS. **7C** and **7D**, the inner wall **50** of the main body **10** is provided with a two-step support rail **144** which extends longitudinally along inside the main body and is located directly adjacent the aperture **74**. As shown in FIG. **7B** a diametrically opposed two-step support rail **146** is also provided and this diametrically opposed in the sense that a vertical plane (not shown) can pass substantially directly through the first rail **144**, the aperture **74**, a central aperture **148** of the valve stem block **40** (in which canister stem **25** is located) and the second two-step support rail **146**. As shown in FIG. **7A** and schematically in FIG. **7B**, the rails **144**, **146** provide a maximum clearance between the canister **20** and the rails **144**, **146** in a radial direction of almost exactly 0.3 mm, about 0.25 to 0.35 mm being a typical range. This clearance in this plane means that the canister **20** can only rock backwards and forwards in this plane towards away from the actuation pin **34**. A relatively small distance and this therefore prevents the canister wobbling and changing the height of the actuation pin **34** as to undesirably alter the accuracy of the dose counter **36**. This is therefore highly advantageous.

The inner wall **50** of the main body **10** is provided with two further two-step rails **150** as well as two pairs **152**, **154** of rails extending different constant radial amounts inwardly from the inner wall **50**, so as to generally achieve a maximum clearance of almost exactly 0.3 mm around the canister **20** for all of the rails **144**, **146**, **150**, **152**, **154** spaced around the periphery of the inner wall **50**, in order to prevent undue rocking while still allowing canister motion freely inside the inhaler **12**. It will be clear from FIG. **7C** for example that the two-step rails have a first portion near an outlet end **156** of the canister chamber **18**, the first portion having a substantially constant radial or inwardly-extending width, a first step **160** leading to a second portion **162** of the rail, the

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second portion **102** having a lesser radial or inwardly extending extent than the first portion **156**, and finally a second step **164** at which the rail merges into the main inner wall **50** main surface.

A method of assembling the inhaler **12** will now be described.

With reference to FIG. **8A**, the main body **10** of the inhaler **12** is formed by two or more plastics mouldings which have been joined together to the configuration shown.

As shown in FIG. **8B**, the actuator pawl **80** and pin **34** are translated forward into position into a pin receiving area **166** in the dose counter chamber **66** and the pin **34** and actuator **80** may then be raised until the pin **34** emerges through the aperture **74**.

Next, the return spring **56** may be inserted below the pin **34** and a generally cylindrical annular lower end **168** of the spring **56** may be moved by a tweezer or tweezer-like assembly tool (not shown) into engagement with a shelf **170** of a spring retainer **172** in the dose counter chamber **66**. The spring retainer **172** is U-shaped and the shelf **170** is U-shaped and has a recess **174** formed below it. As shown in FIGS. **4B**, **4C** and **12** shelf **170** includes three chamfer surfaces **176**, **178**, **180** arranged to assist in moving the lower end of the spring **168** into position onto the shelf using the assembly tool (not shown). Once the lower end of the spring **168** is in place, the assembly tool (not shown) can easily be removed at least partly via the recess **174** below the lower end **168** of the spring **56**.

The tape **112** is attached at one end (not shown) to the tape stock bobbin **110** and is wound onto the bobbin by a motor **200** (FIG. **13**) having a hexagonal output shaft **202** which engages in a hexagonal socket **204** (FIG. **6B**) of the bobbin. During winding, the tape is monitored by a sensor **206**, which may be in the form of a camera or laser scanner, which feeds data to a computer controller **205** for the motor **200**. The controller **205** recognises three positioning markers **210** in the form of lines across the tape **112** and stops the motor **202** when the tape **112** is nearly fully wound onto the bobbin **110**, such that the distal end **212** of the tape **112** can be secured, e.g. by adhesive, to the tape reel shaft **106**. The controller **205** also recognises a pixelated tape size marker **214** observed by the sensor **206** and logs in a stocking system data store **217** details of the tape **112** such as the number of numbers **114** on the tape, such as one hundred and twenty or two hundred numbers **114**. Next, the tape reel shaft is wound until an appropriate position of the lines **210** at which a priming dot **216** will, once the bobbin **110** and reel shaft **106** are slid onto the second shaft **108** and second shaft **104**, be in a position to be located in the window **118** when the inhaler **12** is fully assembled. In the embodiments, the bobbin **110** and reel shaft **106** may be slid onto the shafts **108**, **104** before the tape **112** is secured to the reel shaft **106** and the reel shaft may then be wound to position the priming dot **216**.

Next, the assembled dose counter components of the chassis preassembly **100** shown in FIG. **6B** may as shown in FIG. **8C** be inserted into the dose counter chamber **66**, with pins **182**, **184**, **186** formed on the main body **10** in the dose counter chamber **66** passing through apertures or slots **188**, **190**, **192** formed on the chassis **102**, such that the pins **182**, **184**, **186** extend through (or at least into) the apertures or slots **188**, **190**, **192**. With the chassis **102** being relatively firmly pushed towards the main body **10**, the pins **182**, **184**, **186** are then heat staked and the chassis **102** is therefore after this held very firmly in position in the main body and is unable to move, thereby assisting in providing great accuracy for the dose counter **36**. Next, as shown in FIG. **8D**, the

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dose counter chamber cover **120** may be fitted over the dose counter chamber **66** and may be secured in place such as by welding, with the priming dot **216** being displayed through the window.

The user can, when readying the inhaler **12** for first use, prime the inhaler by depressing the canister **20** three times which will bring the first number **114** on the tape into display through the window **118** in place of the priming dot **216**, the number **114** shown in FIG. **8D** being “200”, thereby indicating that 200 doses are remaining to be dispensed from the canister **20** and inhaler **12**.

As shown in FIG. **8D**, and in FIG. **5**, an open drain hole **194** is provided at the bottom of the dose counter chamber **66** by a substantially semi-circular cut-out or recess formation **196** in a lower surface **198** of the main body **10** of the inhaler. Accordingly, if the user (not shown) should decide to wash the main body **10** of the inhaler, for example after encountering an unhygienic situation or simply as a matter of choice, the drain hole **194** allows initial draining of water from inside the dose counter chamber **66** and also thereafter evaporation of water or any aqueous matter in the dose counter chamber **66** so that the window **118** does not mist up undesirably.

FIG. **14** shows a computer system **230** for designing the dose counter **36** and in particular for calculating distributions representative of average positions and standard deviations in a production series of inhalers of the start, reset, fire, count and end positions of the actuator lower side edge **98** relative to the datum plane **220** (FIG. **9**) and therefore of the actuator pawl **80** generally relative to the ratchet wheel **94**, chassis **102** and, when the inhaler **12** is fully assembled, the main body **10** of the inhaler **12**. The computer system **230** includes a data store **232**, a CPU **234**, an input device **236** (such as a keyboard or communication port) and an output device **238** (such as a communications port, display screen and/or printer). A user may enter data via the input device **236** which may be used by the CPU **234** in a mathematical calculation to predict count failure rates when the various dose counters are to be built in a series with dose counter positions set with given averages and standard deviations and taking into account any momentum/inertia effects and metering valve user-back-pressure reduction effect which will occur upon canister firing of a given type of canister. The computer system **230** is thus mathematically used to design the distributions. For the inhaler **12** described herein with the dose counter **36** and canister **20**, the distributions are designed as shown in FIG. **11**. The x axis shows distance of the lower side surface **98** of the actuator **80** above the datum plane **220** and the y axis is representative of the distribution. Thus, curve **240** shows that the start configuration has an average 1.33 mm above the datum plane **200** (standard deviation is 0.1 mm), curve **242** shows that the reset configuration has an average of 0.64 mm above the datum plane **220** (standard deviation is 0.082 mm), curve **244** shows the fire configuration has an average 0.47 mm below the datum plane **220** (standard deviation is 0.141 mm), curve **246** shows the count configuration has an average 0.95 mm below the datum plane **220** (standard deviation is 0.080 mm), and curve **248** shows the end configuration has an average of 1.65 mm below the datum plane **220** (standard deviation is 0.144 mm).

FIGS. **15** to **20** show a version of the inhaler modified in accordance with the present invention. In these drawings, the same reference numerals have been used to those in the earlier drawings to denote the equivalent components. The inhaler **12** is the same as that in FIGS. **1** to **14** apart from the following modifications.

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First, it can be seen that there is a modification in that the drive teeth **92** of the ratchet wheel **94** have a different profile to that in FIGS. **1** to **14**. There are also only nine ratchet teeth **94** in this embodiment instead of eleven.

Additionally, as shown in FIGS. **18C** and **19C**, the control elements **128**, **130** on the forks **124**, **126** of the second shaft **108** have a tapered profile which is different to the profile of the control elements **128**, **130** shown in FIG. **6F**. Either profile can be used in the embodiment of FIGS. **15** to **20** however.

Furthermore, as shown in FIG. **15**, the tape stock bobbin **110** has an inwardly facing generally cylindrical engagement surface **300** with a wavelike form extending partially therealong. The engagement surface **300** has a cross-section **301** perpendicular to the longitudinal length of the stock bobbin **110** which is constant therealong. This cross-section **301** can be seen in FIG. **16** and consists of a series of ten regularly spaced concavities **302** and ten convex wall portions **304**. The convex wall portions **304** are equi-spaced between the concavities **302**. Each concavity **302** has a radius of 0.2 mm. Each convex wall portion **304** also has a radius of 0.2 mm. Finally, the cross section **301** also includes flat wall portions **306** between all of the radiused wall portions of the concavities **302** and convex wall portions **304**. The geometry of the cross-section **301** is therefore defined by the radii of the concavities **302** and convex wall portions **304**, the flat wall portions **306** and the fact that there are ten concavities **302** and convex wall portions **304**.

The minor diameter of the engagement surface **300**, i.e. between the tips of opposite convex wall portions **304**, is 2.46 mm. The major diameter of the engagement surface **300**, i.e. between the outermost portions of the concavities **302**, is 2.70 mm. The undeformed tip to tip maximum diameter of the forks **124**, **126** of the split pin (the second shaft) **108**, i.e. in the region of the maximum radio extent of the control elements **128**, **130**, is 3.1 millimetres and it will therefore be appreciated that the forks **124**, **126** are resiliently compressed once the stock bobbin **110** has been assembled onto the split pin **108** in all rotational configurations of the stock bobbin **110** relative to the split pin **108**. The minimum gap between the forks **124**, **126** in the plane of the cross sections of FIGS. **18C** and **19C** is 1 mm when the split pin **108** is in the undeformed, pre-inserted state. When the split pin **108** is at maximum compression, as shown in FIGS. **18A** to **18C** when the control elements **128**, **130** are shown to be engaged on top of the convex wall portions **304**, the gap **308** between the tips **310**, **312** of the forks **124**, **126** is 0.36 mm. On the other hand, when the split pin **108** is at minimum compression (once inserted into the stock bobbin) as shown in FIGS. **19A** to **19C**, when the control elements **128**, **130** rest in the concavities **302**, the gap between the tips **310**, **312** of the forks **124**, **126** is 0.6 mm. The control elements **128**, **130** are outwardly radiused with a radius also of 0.2 mm such that they can just rest on the concavities **302** with full surface contact (at least at an axial location on the split pin where the tapered control elements are at their maximum radial extent), without rattling in, locking onto or failing to fit in the concavities **302**. The radii of the control elements **128**, **130** is therefore preferably substantially the same as the radii of the concavities **302**.

It will be appreciated that whereas FIGS. **18B** and **19B** are end views along the coaxial axis of the stock bobbin **110** and split pin **108**, FIGS. **18A** and **19A** are cross-sections. FIG. **19A** is a section on the plane A-A' in FIG. **19C** and FIG. **18A** is a section at the same plane, but of course with the stock bobbin **110** rotated relative to the split pin **108**.

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As the inhaler 12 is used and the ratchet wheel 94 rotates in order to count used doses, the stock bobbin rotates incrementally through rotational positions in which rotation is resisted, i.e. due to increasing compression of the split pin 108 at such rotational positions, and rotational positions in which rotation is promoted, i.e. due to decreasing compression of the split pin 108 at such rotational positions and this may involve a click forward of the stock bobbin 110 to the next position equivalent to that in FIGS. 19A to 19C in which the control elements 128, 130 of the split pin art located in the concavities 302. This functionality firstly allows the stock bobbin to unwind during use as required, but also prevents the tape 112 from loosening during transit if the inhaler 12 is dropped, such as onto a hard surface. This is highly advantageous, since the tape 11 is prevented from moving to a position in which it will give an incorrect reading regarding the number of doses in the canister.

During compression and expansion of the forks in the radial direction between the two configurations shown in FIGS. 18C and 19C, the forks 124, 126 rotate about a point 316 on the split pin where the forks 124, 126 come together. This rotational action means that there is a camming action between the forks 124, 126 and the engagement surface 300 without significant friction but, nevertheless, the resilient forces provided by the regulator formed by the engagement surface 300 and forks 124, 126 are able to regulate unwinding of the tape such that it does not easily occur during transit or if the inhaler 12 is dropped. It has been found during testing that a force of 0.3 to 0.4 N needs to be applied to the tape 112 to overcome the regulator at the stock bobbin 110. 0.32 N is achieved with the control elements 128 having the profile shown in FIG. 19C and 0.38 N is achieved with the profile of the control elements 128 altered to be as shown as described with reference to FIG. 6F. These forces are substantially higher than the 0.1 N force mentioned above and undesirable movement of the tape is substantially avoided even if the inhaler is dropped onto a hard surface. The modified arrangement of FIGS. 15 to 20 does not provide this force "constantly" such that there is overall not an undesirably high friction of the tape 112 as it passes over the other components of the dose counter because, due to the incremental nature of the resilient forces at the regulator, the tape 112 can incrementally relax as it slides over the stationary chassis components.

Instead of having ten concavities 302 and convex wall portions 304, other numbers may be used, such as 8 or 12. However, it is preferred to have an even number, especially since two control elements 128, 130 are provided, so that all of the control elements 128, 130 will expand and contract simultaneously. However, other arrangements are envisaged with 3 or more forks and the number of concavities/convex wall portions may be maintained as an integer divisible by the number of forks to maintain a system with simultaneous expansion/contraction. For example, the use of 9, 12 or 15 concavities/convex wall portions with 3 forks is envisaged.

Instead of having the engagement surface 300 on the inside of the stock bobbin 110, it could be placed on the outside of the stock bobbin 110 so as to be engaged by flexible external legs/pawls or similar.

It will be noted that the regulator provided by the engagement surface 300 and forks 124, 126 does not only allow rotation of the stock bobbin in one direction as is the case with the ratchet wheel 94. Rotation in both directions is possible, i.e. forwards and backwards. This means that during assembly, the stock bobbin 110 can be wound backwards during or after fitting the bobbin 100, shaft 106 and tape 112 onto the carriage 102, if desired.

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The stock bobbin 110 and the carriage 102 including the split pin 108 are both moulded of polypropylene material.

It will be seen from FIG. 16 that the cross-sectional shape 301 is not symmetrical within the hexagonal socket 204. This has enabled the hexagonal socket 204 to be maintained at a useful size while still allowing the desired size and geometry of the cross section 301 to fit without interfering with the hexagonal shape of the hexagonal socket 204 and also permits moulding to work during manufacture.

As shown in FIG. 17, the stock bobbin 110 has a series of four circumferential ribs 330 inside it and a spaced therealong. These hold the stock bobbin 110 on the correct side of the mould tool during moulding.

FIGS. 21 and 22 show a preferred embodiment in accordance with the invention of an inhaler 510 for dispensing a dry-powdered medicament in metered doses for patient inhalation. The inhaler 510 is as disclosed in FIGS. 1 to 16 or EP-A-1330280, the contents of which are hereby fully incorporated herein by reference, but with the stock bobbin 110 and second shaft 108 of the dose counter 516 modified so as to be as in FIGS. 15 to 20 hereof. Thus, the dry powder inhaler 510 generally includes a housing 518, and an assembly 512 received in the housing (see FIG. 21). The housing 518 includes a case 520 having an open end 522 and a mouthpiece 524 (FIG. 25) for patient inhalation, a cap 526 secured to and closing the open end 522 of the case 520, and a cover 528 pivotally mounted to the case 520 for covering the mouthpiece 524. As shown in FIG. 22, the inhaler 510 also includes an actuation spring 569, first yoke 566 with opening 572, bellows 540 with crown 574, a reservoir 514, second yoke 568 with hopper 542 and dose counter 516 mounted thereto, and case 520 has transparent window 5130 thereon for viewing dose counter tape indicia 5128. The dose metering system also includes two cams 570 mounted on the mouthpiece cover 528 and movable with the cover 528 between open and closed positions. The cams 570 each include an opening 580 for allowing outwardly extending hinges 582 of the case 520 to pass therethrough and be received in first recesses 584 of the cover 528. The cams 570 also include bosses 586 extending outwardly and received in second recesses 588 of the cover 528, such that the cover 528 pivots about the hinges 582 and the cams 570 move with the cover 528 about the hinges 582. As described in EP-A-1330280, cams 570 act upon cam followers 578 to move second yoke 568 up and down and thereby operate dose counter by engagement of pawl 5138 on the second yoke 568 with teeth 5136. Remaining components of the inhaler are provided as, and operate as described, in EP-A-1330280.

The dose counting system 516 therefore includes a ribbon or tape 5128 (FIGS. 23 & 24), having successive numbers or other suitable indicia printed thereon, in alignment with a transparent window 5130 provided in the housing 18 (see FIG. 22). The dose counting system 516 includes the rotatable stock bobbin 110 (as described above), an indexing spool 5134 rotatable in a single direction, and the ribbon 5128 rolled and received on the bobbin 110 and having a first end 5127 secured to the spool 5134, wherein the ribbon 5128 unrolls from the bobbin 110 so that the indicia are successively displayed as the spool 5134 is rotated or advanced. In FIGS. 23 and 24 the wavelike engagement surface 300 of the bobbin 110 is not shown for the purposes of clarity.

The spool 134 is arranged to rotate upon movement of the yokes 566, 568 to effect delivery of a dose of medicament from reservoir 514, such that the number on the ribbon 5128 is advanced to indicate that another dose has been dispensed by the inhaler 510. The ribbon 5128 can be arranged such that the numbers, or other suitable indicia, increase or

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decrease upon rotation of the spool 5134. For example, the ribbon 5128 can be arranged such that the numbers, or other suitable indicia, decrease upon rotation of the spool 5134 to indicate the number of doses remaining in the inhaler 510. Alternatively, the ribbon 5128 can be arranged such that the numbers, or other suitable indicia, increase upon rotation of the spool 5134 to indicate the number of doses dispensed by the inhaler 10.

The indexing spool 5134 includes radially extending teeth 5136, which are engaged by pawl 5138 extending from a cam follower 578 of the second yoke 568 upon movement of the yoke to rotate, or advance, the indexing spool 5134. More particularly, the pawl 5138 is shaped and arranged such that it engages the teeth 5136 and advances the indexing spool 5134 only upon the mouthpiece cover 528 being closed and the yokes 566, 568 moved back towards the cap 526 of the housing 518.

The dose counting system 516 also includes a chassis 5140 that secures the dose counting system to the hopper 542 and includes shafts 108, 5144 for receiving the bobbin 110 and the indexing spool 5134. As described above with reference to FIGS. 1 to 20, the bobbin shaft 108 is forked and includes radially nubs 5146 for creating a resilient resistance to rotation of the bobbin 110 on the shaft 108 by engaging with the wavelike engagement surface 300 inside the bobbin 110. A clutch spring 5148 is received on the end of the indexing spool 5134 and locked to the chassis 5140 to allow rotation of the spool 5134 in only a single direction.

Various modifications may be made to the embodiment shown without departing from the scope of the invention as defined by the accompanying claims as interpreted under patent law.

What is claimed is:

1. A dose counter for an inhaler, the dose counter having a counter display arranged to indicate dosage information, a drive system arranged to move the counter display incrementally in a first direction from a first station to a second station in response to actuation input, wherein a regulator is provided which is arranged to act upon the counter display at the first station to regulate motion of the counter display at the first station to incremental movements.

2. The dose counter as claimed in claim 1 in which the counter display comprises a tape.

3. The dose counter as claimed in claim 2 in which the tape has dose counter indicia displayed thereon.

4. The dose counter as claimed in claim 2 wherein the first station comprises a first shaft, the tape being arranged on the first shaft and to unwind therefrom upon movement of the counter display.

5. The dose counter as claimed in claim 4 in which the first shaft is mounted for rotation relative to a substantially rotationally fixed element of the dose counter.

6. The dose counter as claimed in claim 5 in which the regulator comprises at least one projection on one of the first shaft and the substantially rotationally fixed element, which is arranged to engage incrementally with one or more formations on the other of the substantially rotationally fixed element and the first shaft.

7. The dose counter as claimed in claim 6 in which at least two said projections are provided.

8. The dose counter as claimed in claim 6 in which exactly two said projections are provided.

9. The dose counter as claimed in claim 6 in which each projection comprises a radiused surface.

10. The dose counter as claimed in claim 6 in which the at least one projection is located on the substantially rota-

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tionally fixed element which comprises a fixed shaft which is fixed to the main body of the dose counter, the first shaft being rotationally mounted to the fixed shaft.

11. The dose counter as claimed in claim 10 in which the fixed shaft has at least two flexible legs, and each leg has at least one said projection formed in an outwardly facing direction thereon, said one or more formations being formed on an inwardly facing engagement surface of the first shaft, said at least one projection being arranged to resiliently engage said one or more formations.

12. The dose counter as claimed in claim 10 in which the fixed shaft comprises a split pin with fork legs and in which each projection is located on a said fork leg.

13. The dose counter as claimed in claim 6 in which a series of said formations are provided.

14. The dose counter as claimed in claim 6 in which an even number of said formations is provided.

15. The dose counter as claimed in claim 6 in which from eight to twelve of said formations are provided.

16. The dose counter as claimed in claim 15 in which ten of said formations are provided.

17. The dose counter as claimed in claim 6 in which each said formation comprises a concavity formed on an engagement surface.

18. The dose counter as claimed in claim 17 in which each concavity comprises a radiused surface wall portion which merges on at least one side thereof into a flat wall portion surface.

19. The dose counter as claimed in claim 18 in which the engagement surface includes a series of said concavities and in which convex wall portions of the engagement surface are formed between each adjacent two said concavities, each said convex wall portion comprising a convex radiused wall portion.

20. The dose counter as claimed in claim 19 in which each convex radiused wall portion of each convex wall portion is connected by said flat wall portion surfaces to each concavity which is adjacent thereto.

21. The dose counter as claimed in claim 4 in which the first shaft comprises a substantially hollow bobbin.

22. The dose counter as claimed in claim 21 in which said one or more formations are located on an inner surface of the bobbin.

23. The dose counter as claimed in claim 4 wherein the drive system comprises a tooth ratchet wheel arranged to act upon a second shaft which is located at the second station, the second shaft being rotatable to wind the tape onto the second shaft.

24. The dose counter as claimed in claim 23 in which the second shaft is located on the main body of the dose counter spaced from and parallel to the first shaft.

25. The dose counter as claimed in claim 23 in which the tooth ratchet wheel is fixed to the second shaft and is arranged to rotate therewith.

26. The dose counter as claimed in claim 23 which includes an anti-back drive system which is arranged to restrict motion of the second shaft in a tape winding direction.

27. The dose counter as claimed in claim 1 in which the regulator provides a resistance force of greater than 0.1 N against movement of the counter display.

28. The dose counter as claimed in claim 27 in which the resistance force is greater than 0.3 N.

29. The dose counter as claimed in claim 27 in which the resistance force is from 0.3 to 0.4 N.

* * * * *

EXHIBIT G

US010695512B2

(12) **United States Patent**
Walsh et al.(10) **Patent No.:** **US 10,695,512 B2**(45) **Date of Patent:** ***Jun. 30, 2020**(54) **DOSE COUNTER FOR INHALER HAVING
AN ANTI-REVERSE ROTATION ACTUATOR**(71) Applicants: **Ivax Pharmaceuticals Ireland,**
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(IE)(*) Notice: Subject to any disclaimer, the term of this
patent is extended or adjusted under 35
U.S.C. 154(b) by 302 days.

This patent is subject to a terminal dis-
claimer.(21) Appl. No.: **15/804,735**(22) Filed: **Nov. 6, 2017**(65) **Prior Publication Data**

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Related U.S. Application Data(60) Continuation of application No. 15/269,249, filed on
Sep. 19, 2016, now Pat. No. 9,808,587, which is a
(Continued)(51) **Int. Cl.****A61M 15/00** (2006.01)**G06M 1/24** (2006.01)**A61M 11/00** (2006.01)(52) **U.S. Cl.**CPC **A61M 15/0078** (2014.02); **A61M 11/00**
(2013.01); **A61M 15/007** (2014.02);
(Continued)(58) **Field of Classification Search**CPC **A61M 15/0078**; **A61M 15/0025**; **A61M**
15/0026; **A61M 15/007**; **A61M 15/0071**
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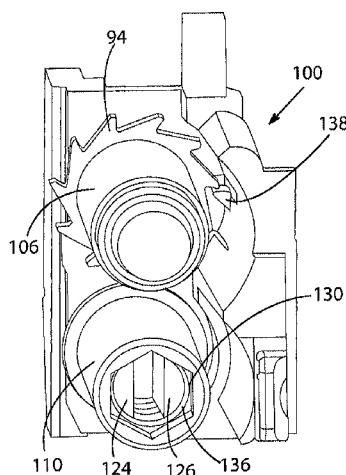
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(Continued)*Primary Examiner* — Daniel A Hess(74) *Attorney, Agent, or Firm* — Morgan, Lewis &
Bockius LLP(57) **ABSTRACT**An inhaler includes a main body having a canister housing,
a medicament canister retained in a central outlet port of the
canister housing, and a dose counter having an actuation
member for operation by movement of the medicament
canister. The canister housing has an inner wall, and a first
inner wall canister support formation extending inwardly
from a main surface of the inner wall. The canister housing

(Continued)



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has a longitudinal axis X which passes through the center of the central outlet port. The first inner wall canister support formation, the actuation member, and the central outlet port lie in a common plane coincident with the longitudinal axis X such that the first inner wall canister support formation protects against unwanted actuation of the dose counter by reducing rocking of the medicament canister relative to the main body of the inhaler.

6 Claims, 17 Drawing Sheets**Related U.S. Application Data**

continuation of application No. 14/103,324, filed on Dec. 11, 2013, now Pat. No. 9,463,289, which is a division of application No. 13/110,532, filed on May 18, 2011, now Pat. No. 8,978,966.

- (60) Provisional application No. 61/417,659, filed on Nov. 29, 2010, provisional application No. 61/345,763, filed on May 18, 2010.

(52) **U.S. Cl.**

CPC *A61M 15/009* (2013.01); *A61M 15/0025* (2014.02); *A61M 15/0026* (2014.02); *A61M 15/0065* (2013.01); *A61M 15/0071* (2014.02); *G06M 1/246* (2013.01); *A61M 2202/064* (2013.01); *A61M 2205/6063* (2013.01); *A61M 2207/00* (2013.01); *A61M 2207/10* (2013.01); *Y10T 29/49* (2015.01); *Y10T 29/49764* (2015.01); *Y10T 29/49826* (2015.01)

(58) **Field of Classification Search**

USPC 128/203.12
See application file for complete search history.

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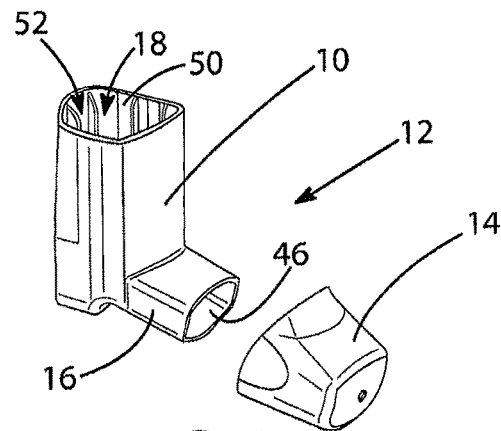


FIG. 1

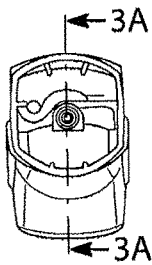


FIG. 2

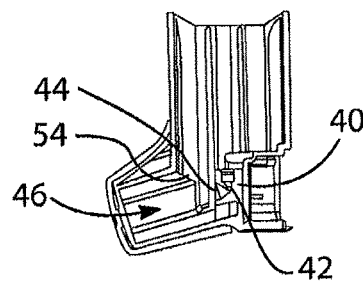


FIG. 3A

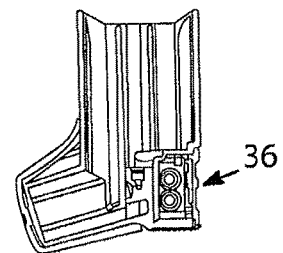


FIG. 3B

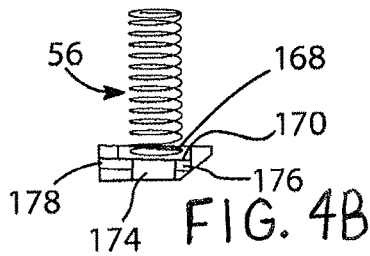


FIG. 4B

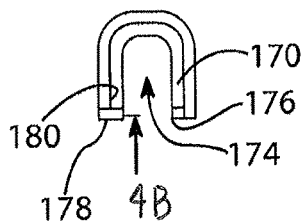


FIG. 4C

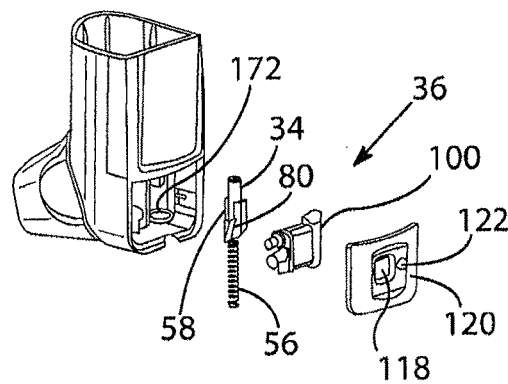


FIG. 4A

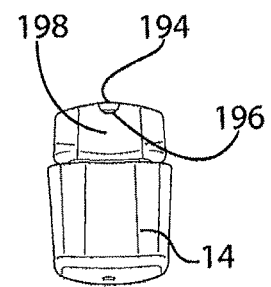


FIG. 5

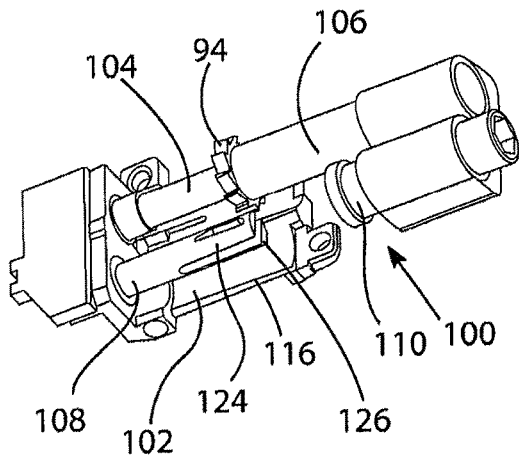


FIG. 6A

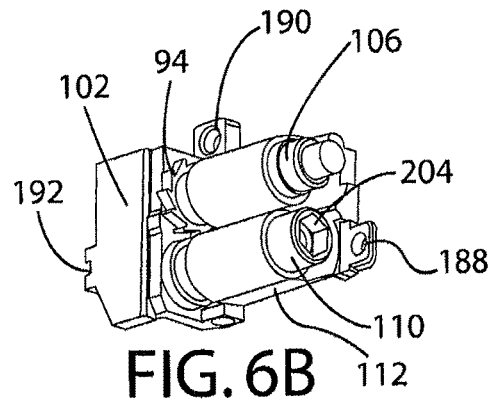


FIG. 6B

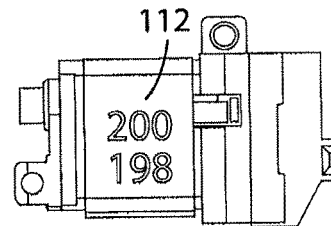


FIG. 6C

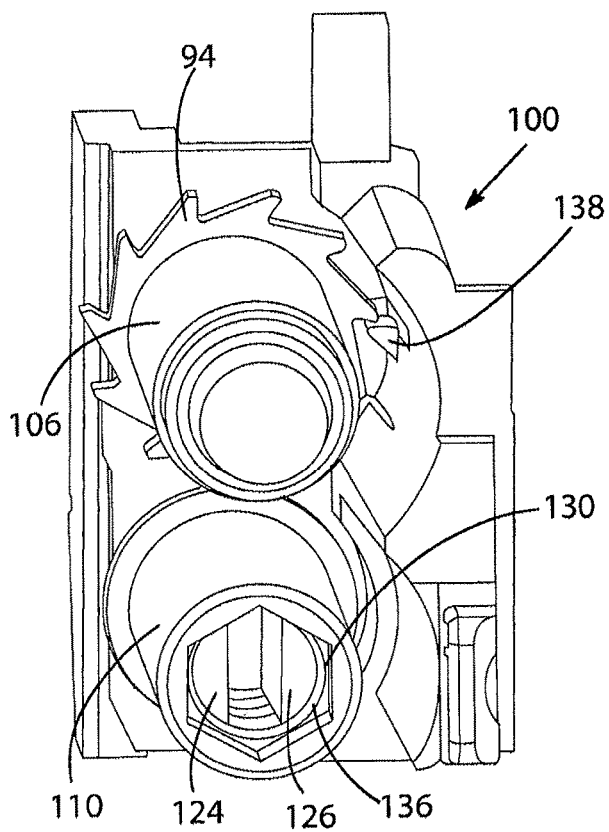


FIG. 6D

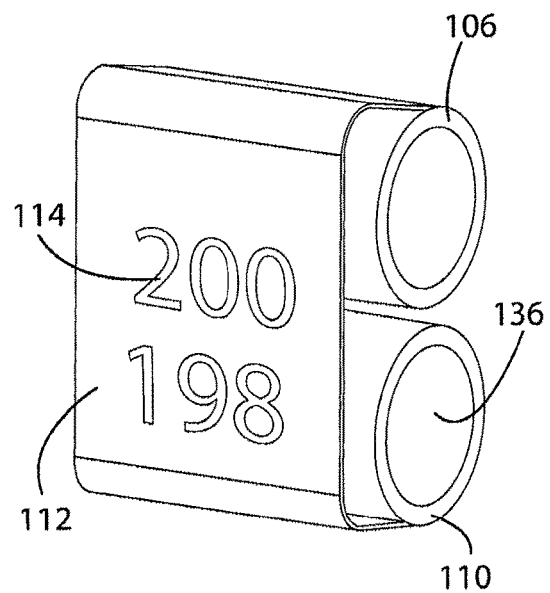


FIG. 6E

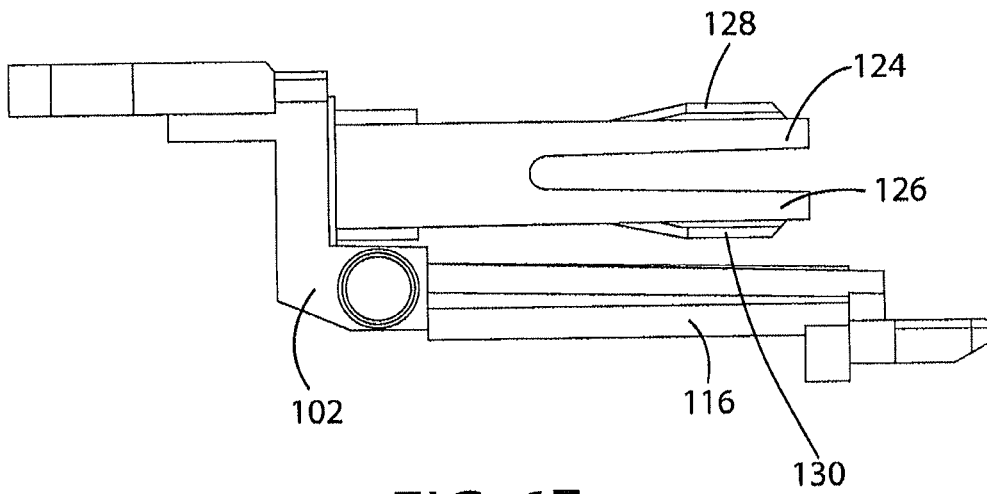


FIG. 6F

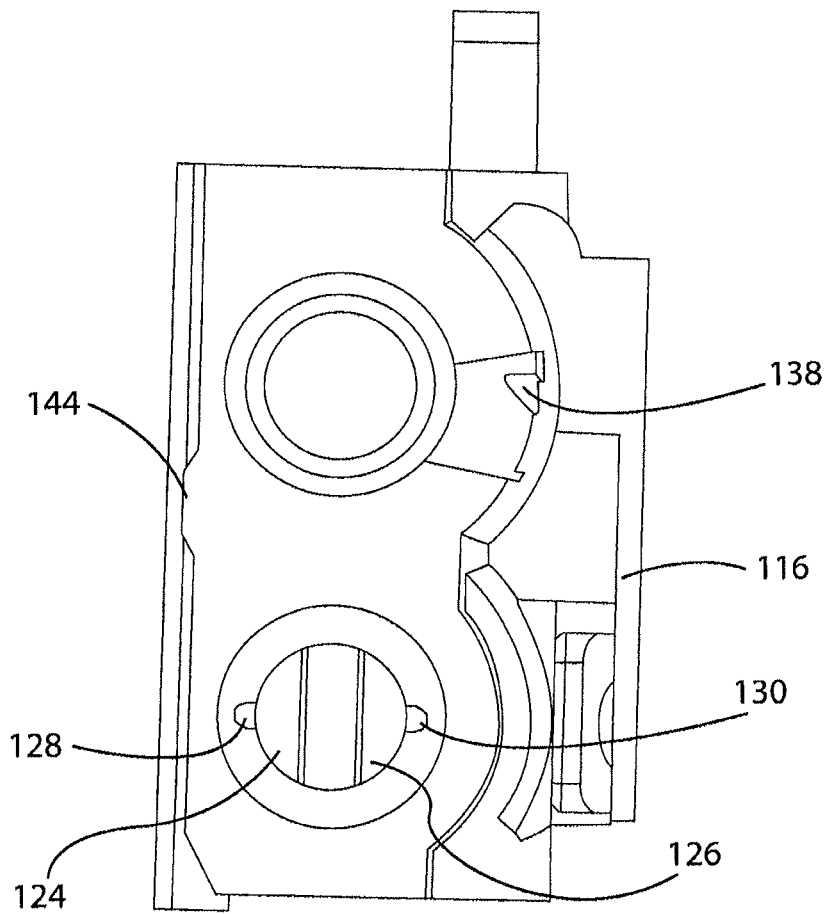


FIG. 6G

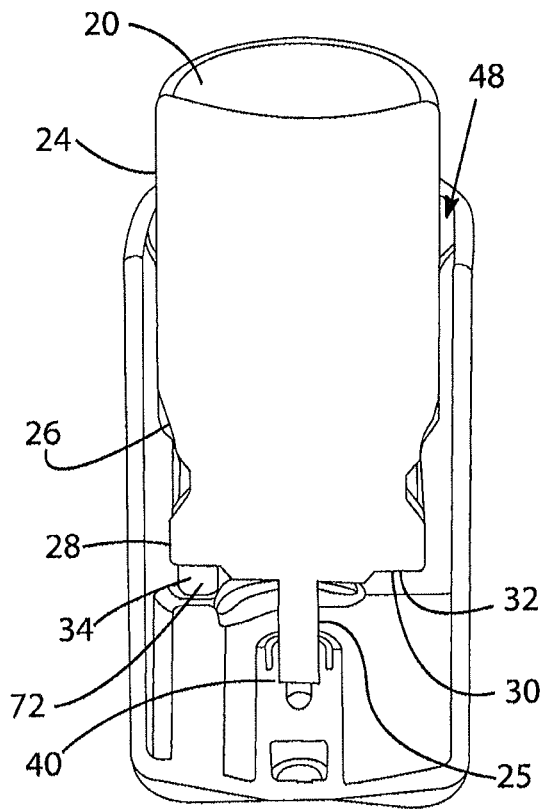


FIG. 7A

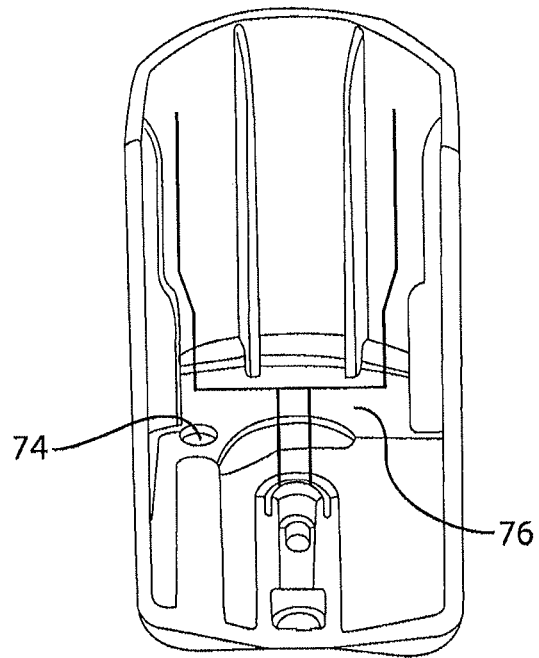


FIG. 7B

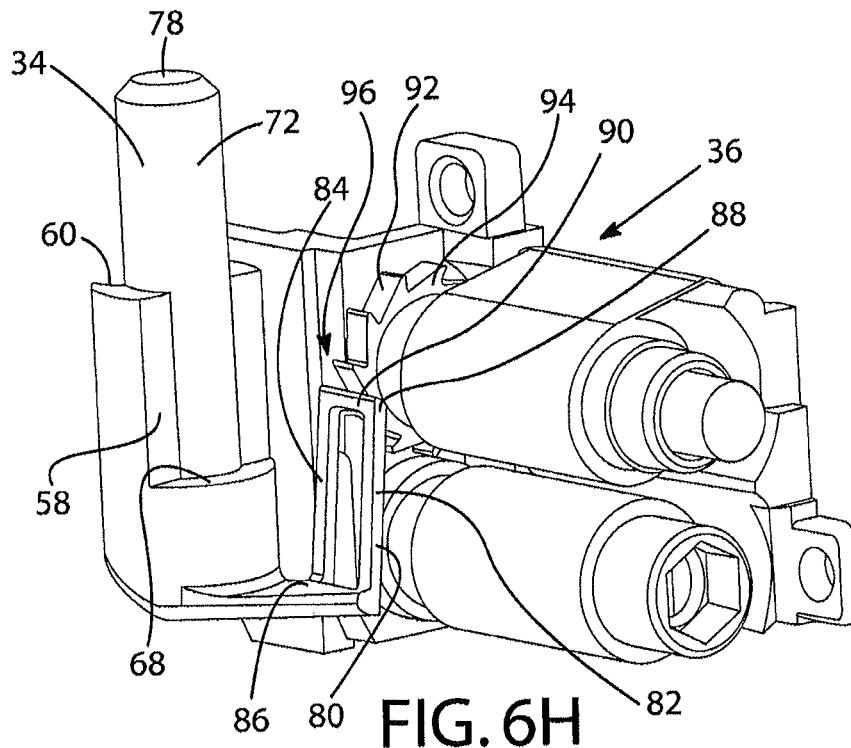


FIG. 6H

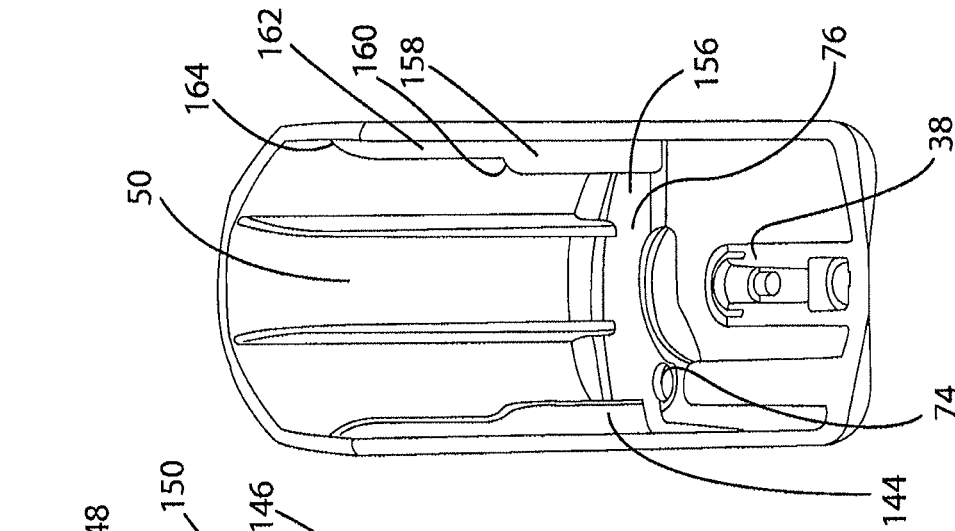


FIG. 7C

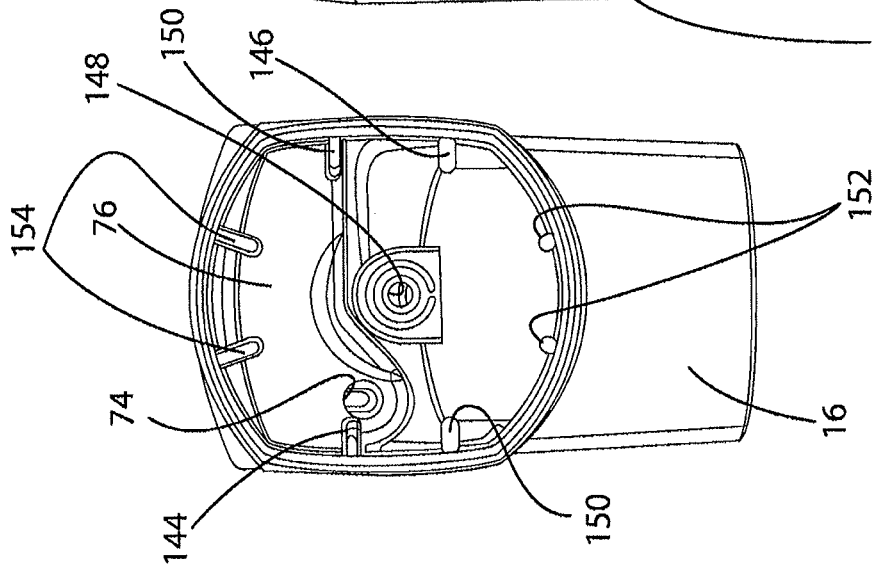


FIG. 7D

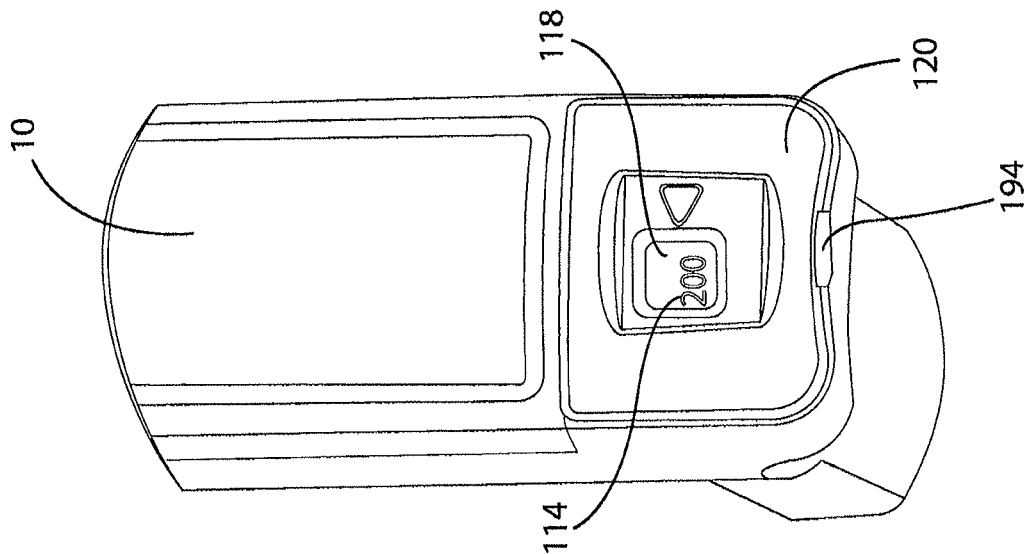


FIG. 8D

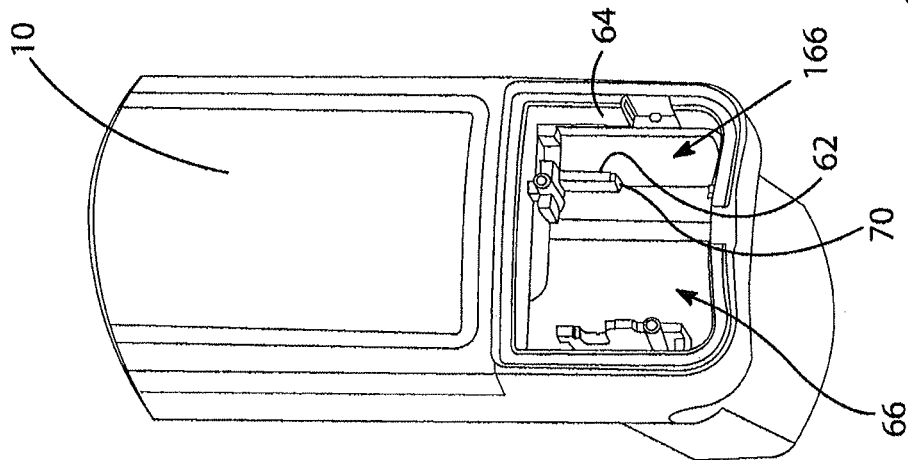


FIG. 8A

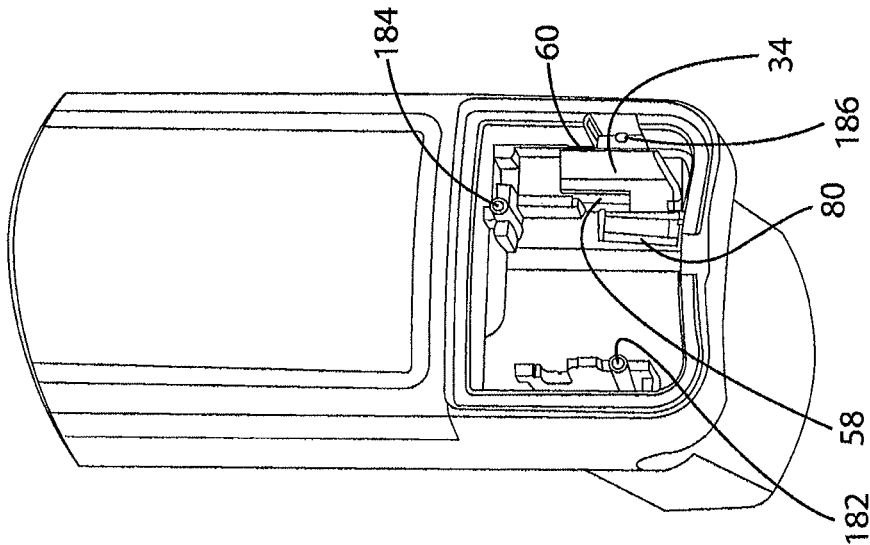


FIG. 8B

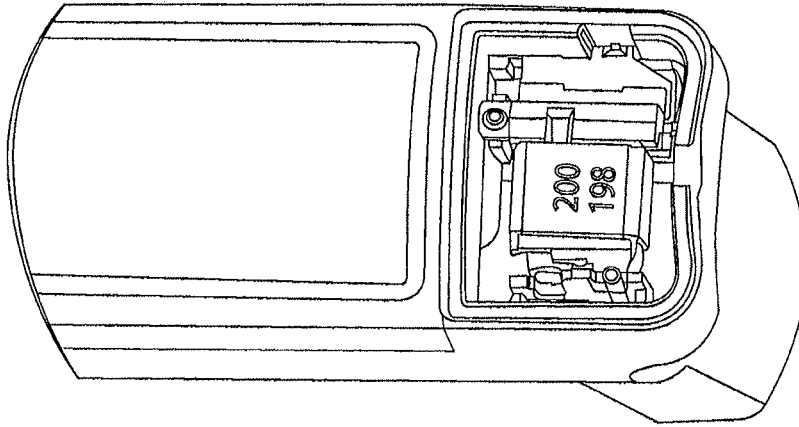


FIG. 8C

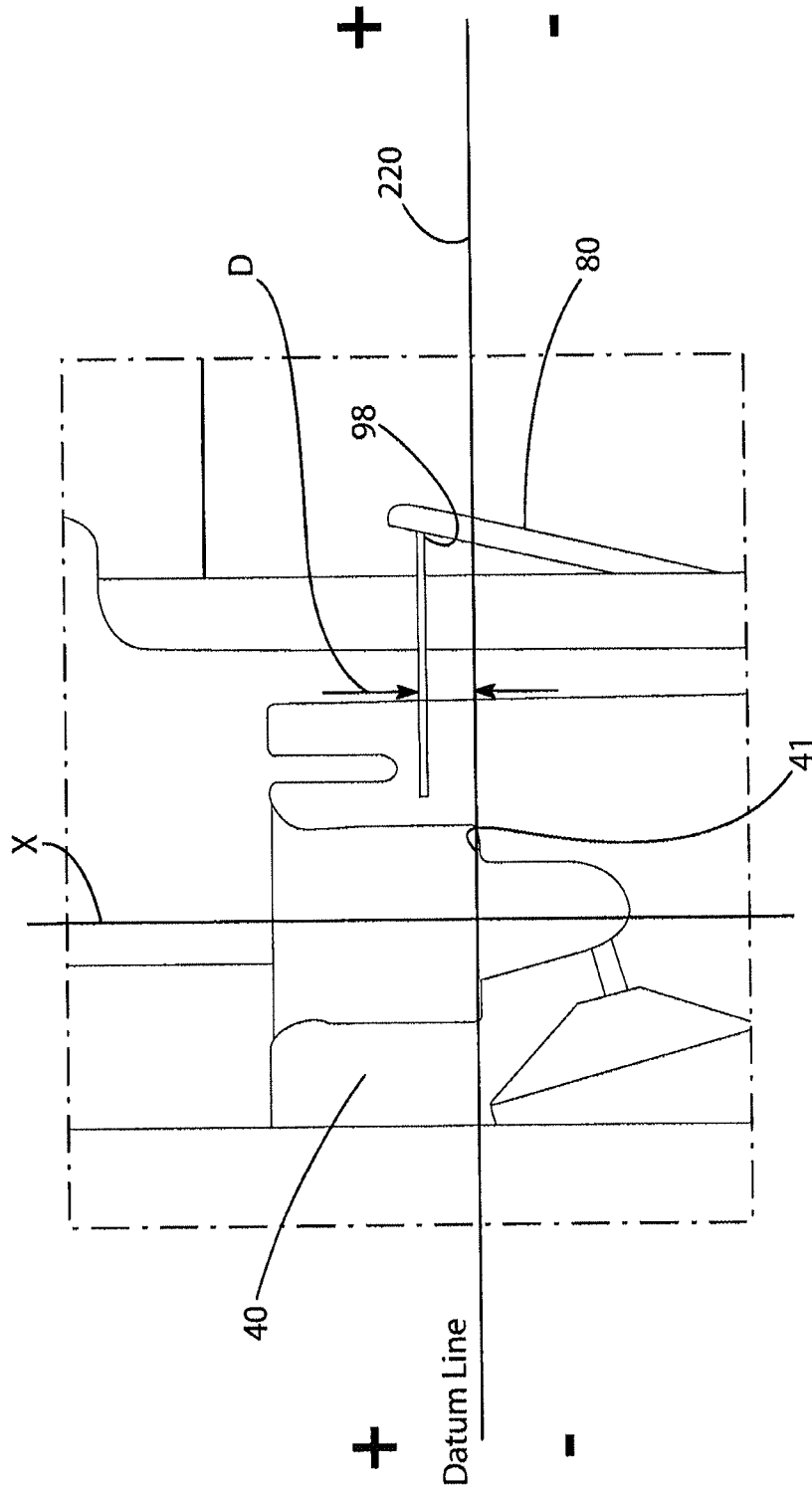
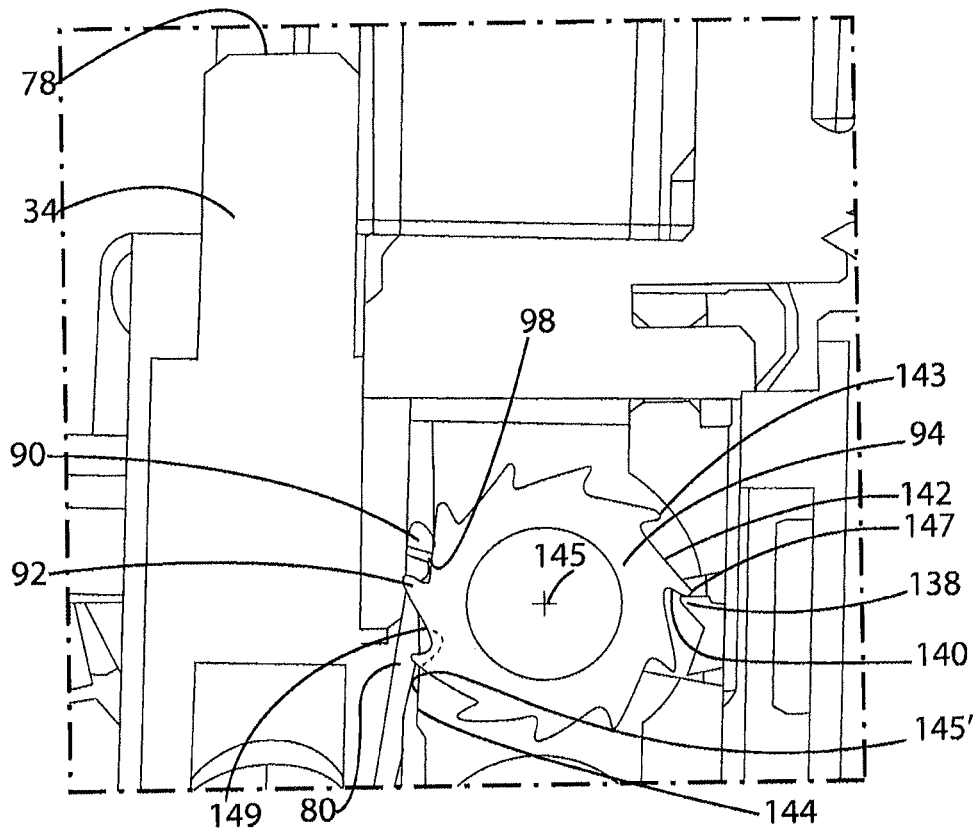
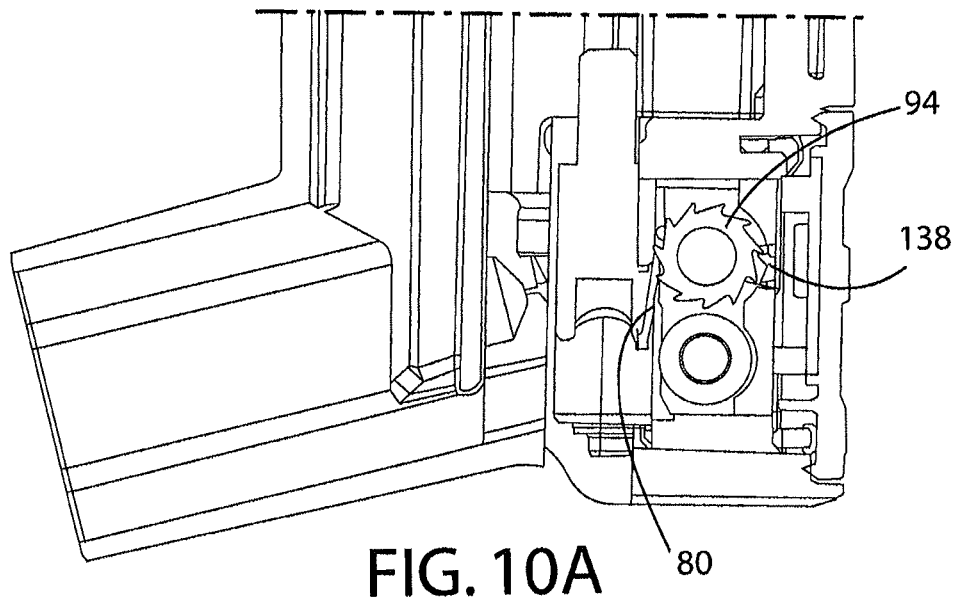


FIG. 9



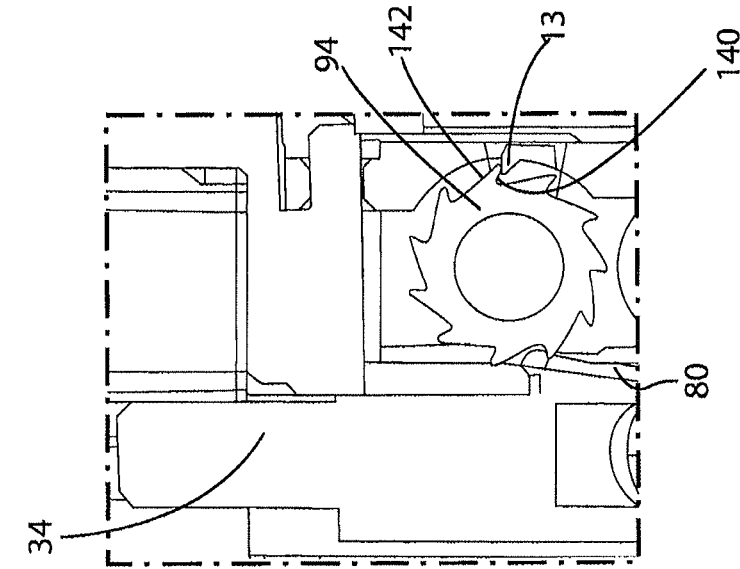


FIG. 10E

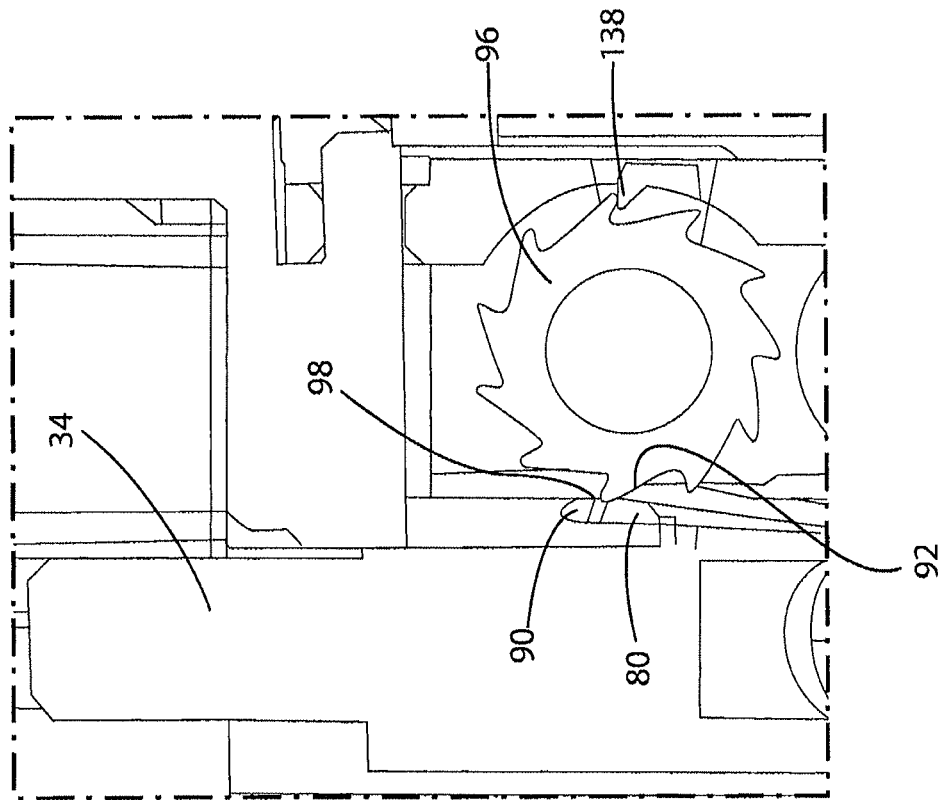


FIG. 10C

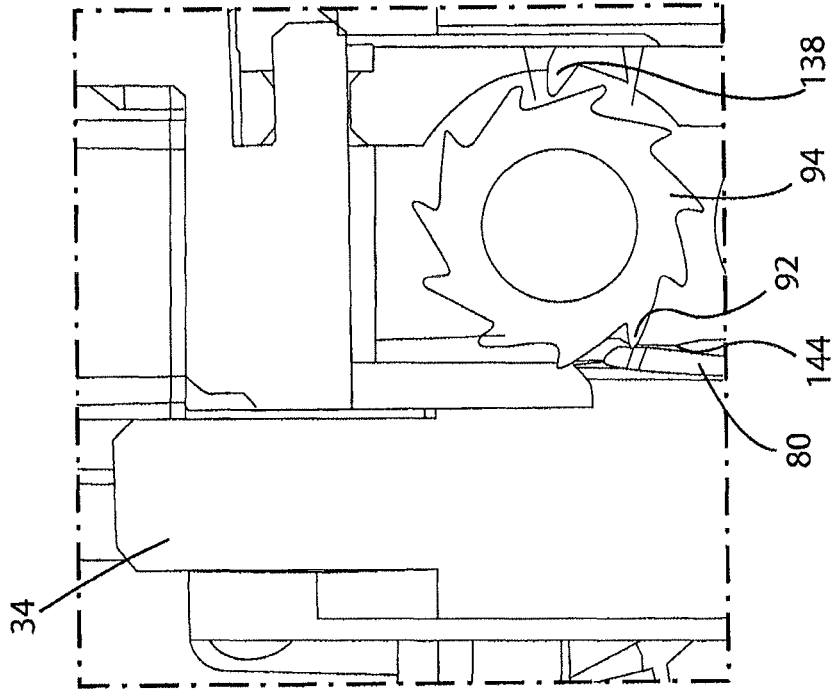


FIG. 10F

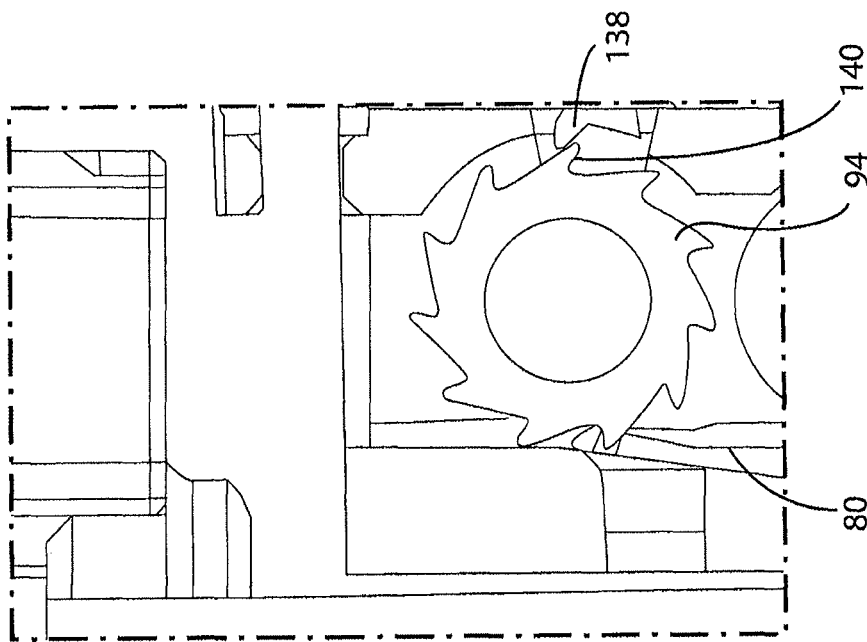


FIG. 10D

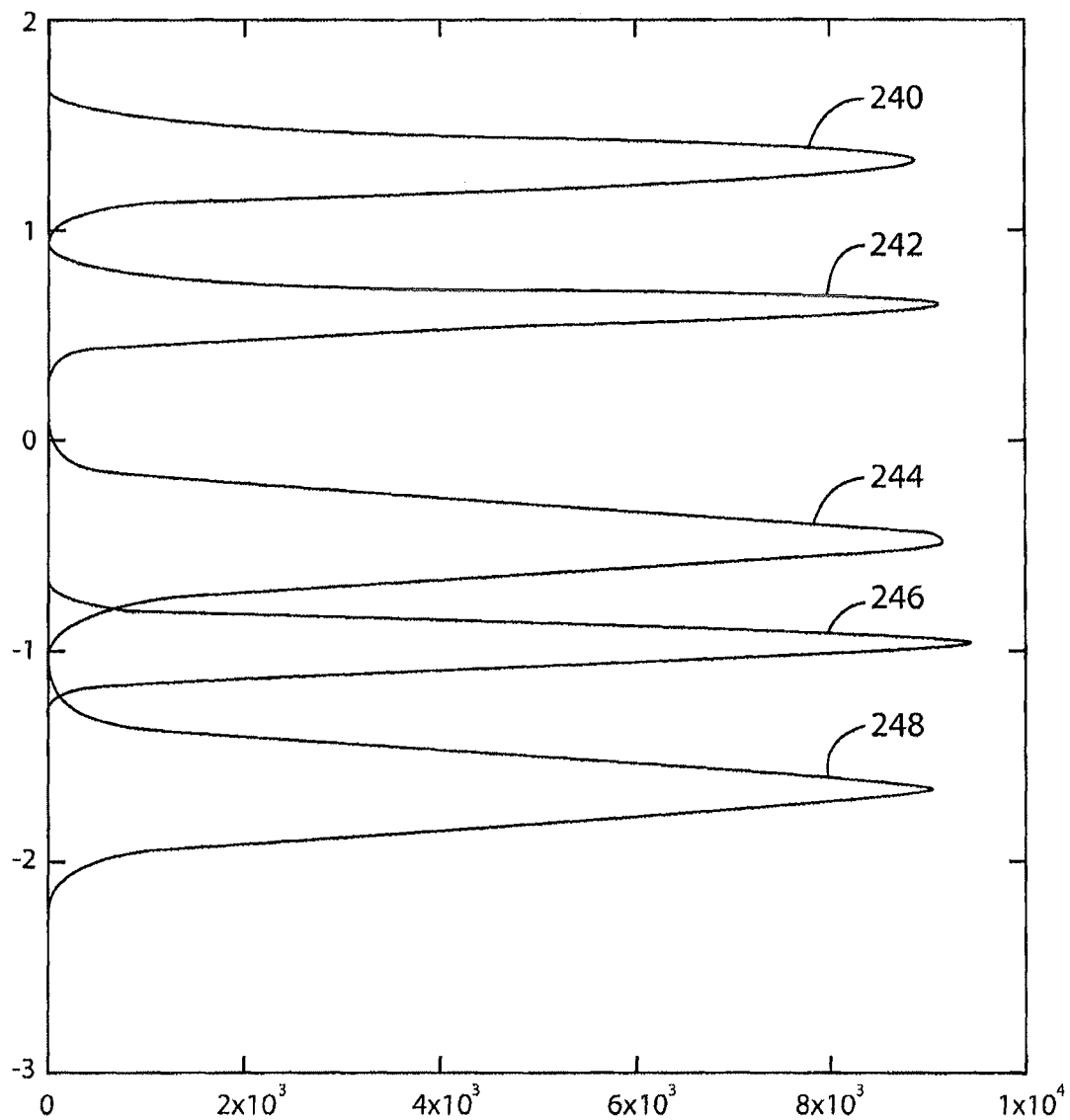


FIG. 11

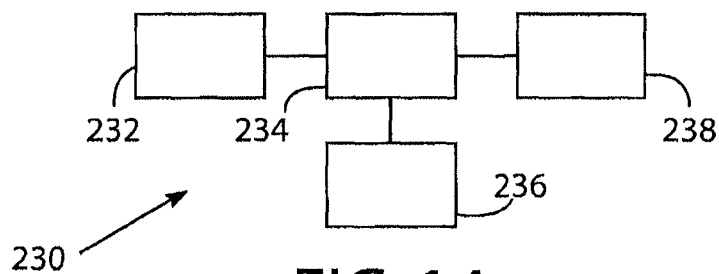


FIG. 14

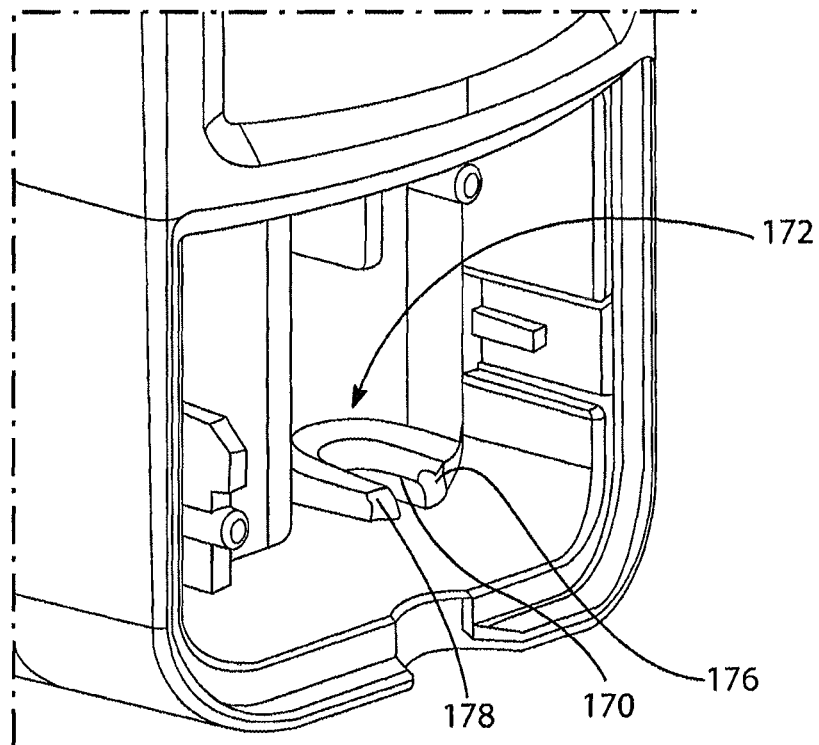


FIG. 12

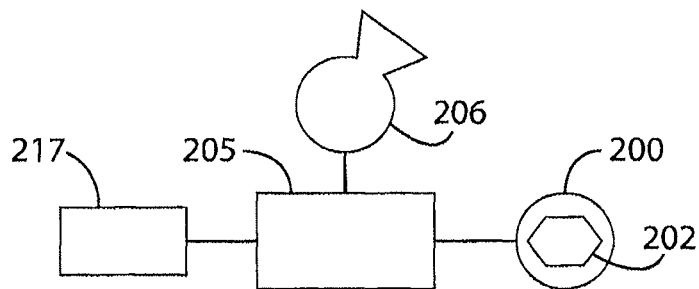
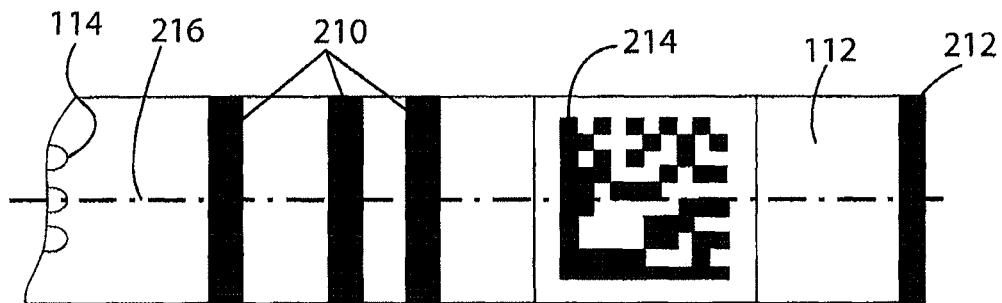


FIG. 13

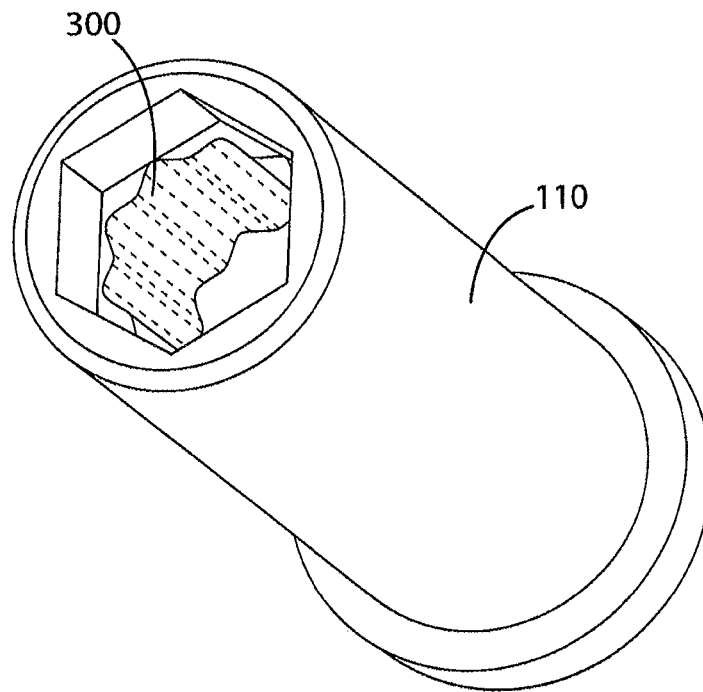


FIG. 15

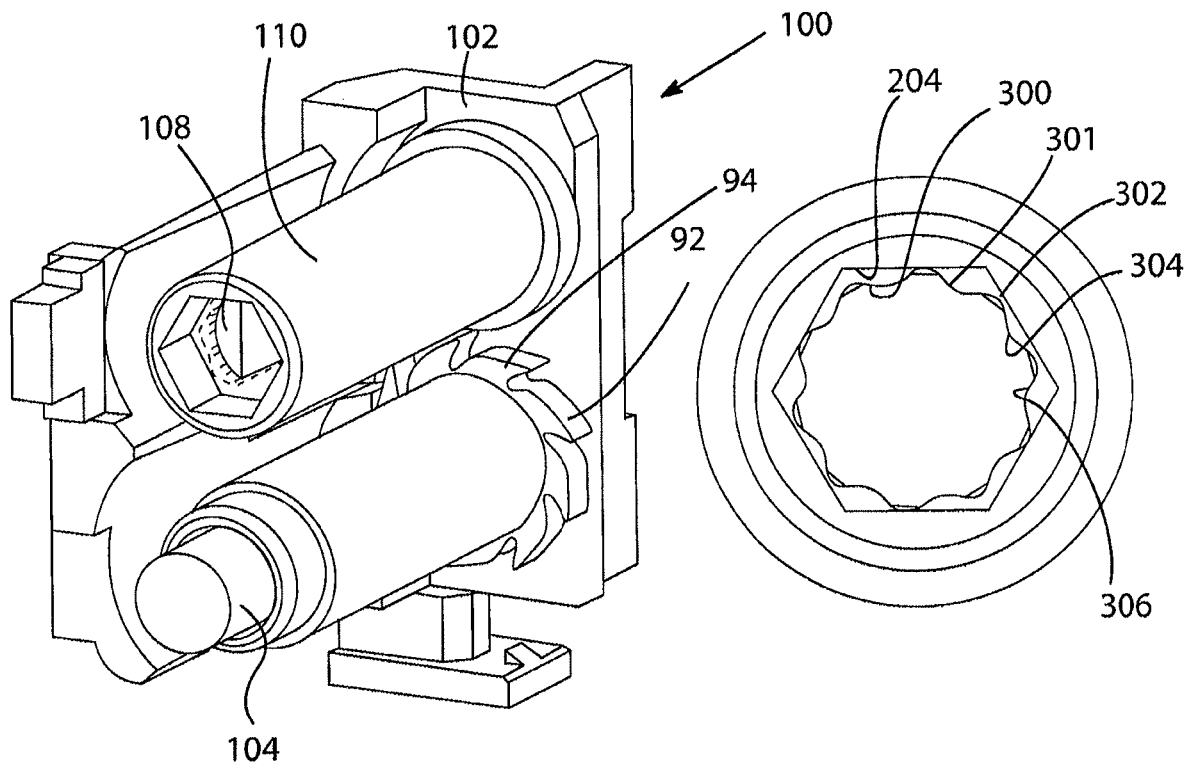


FIG. 20

FIG. 16

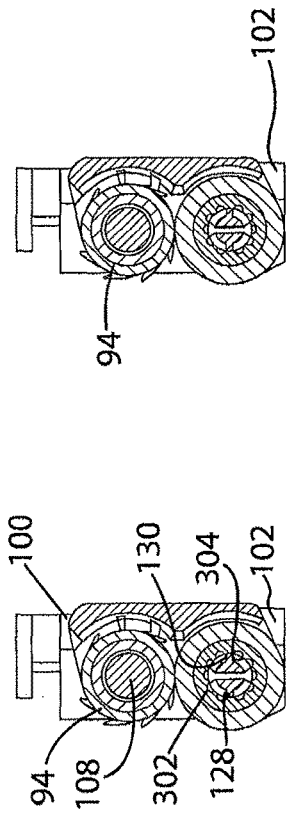


FIG. 18A

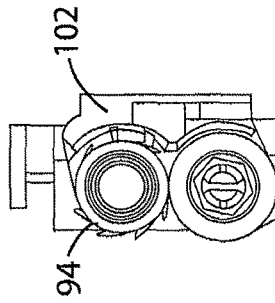


FIG. 18B

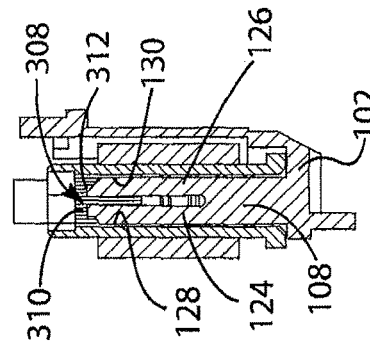


FIG. 18C

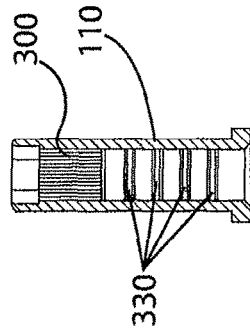


FIG. 17

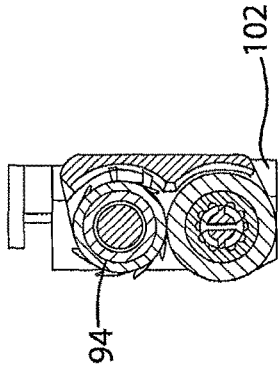


FIG. 19A

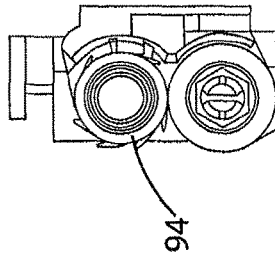


FIG. 19B

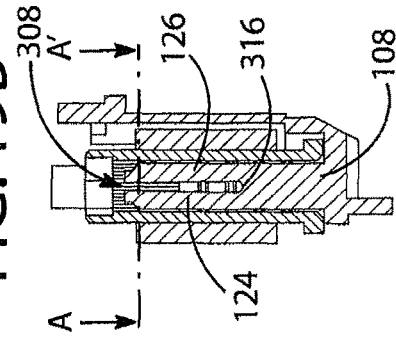


FIG. 19C

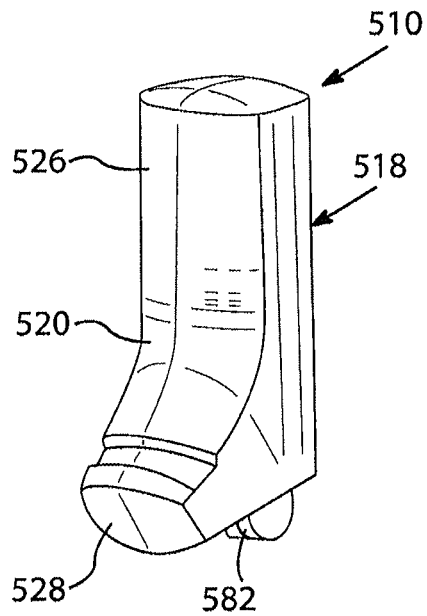


FIG. 21

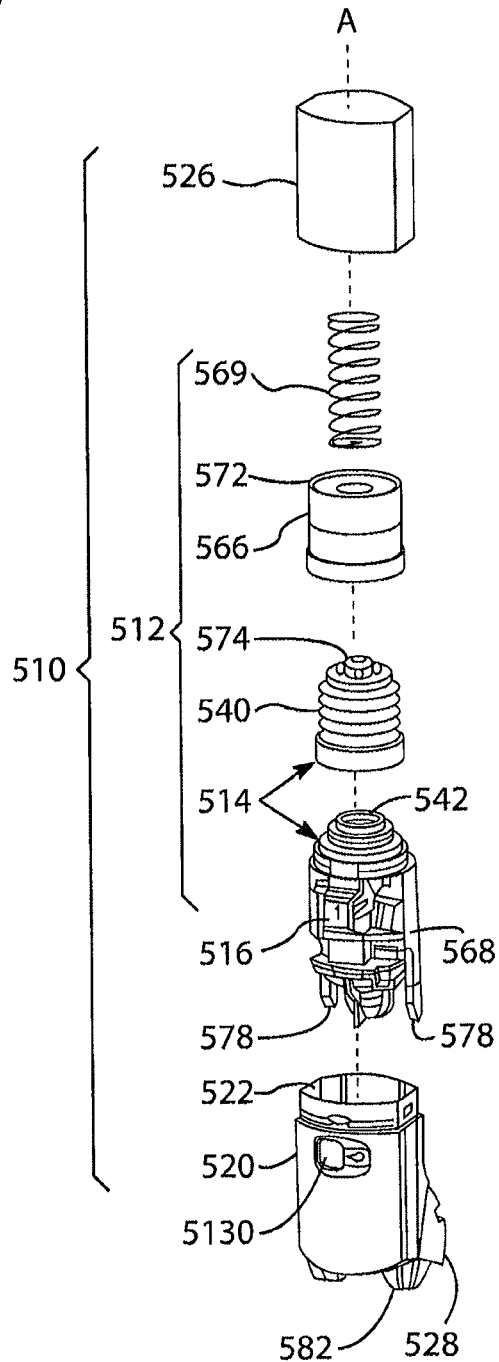


FIG. 22

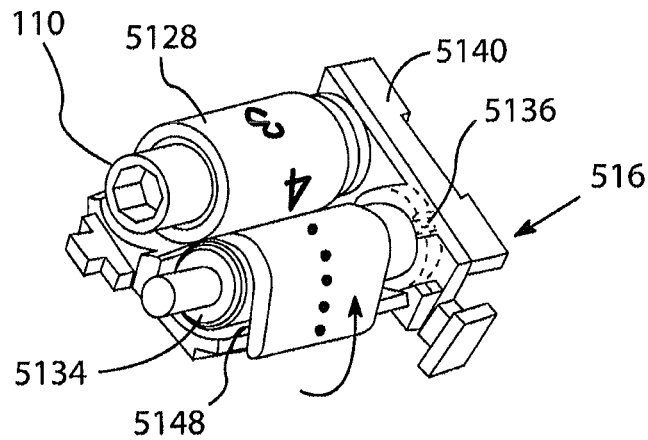


FIG. 23

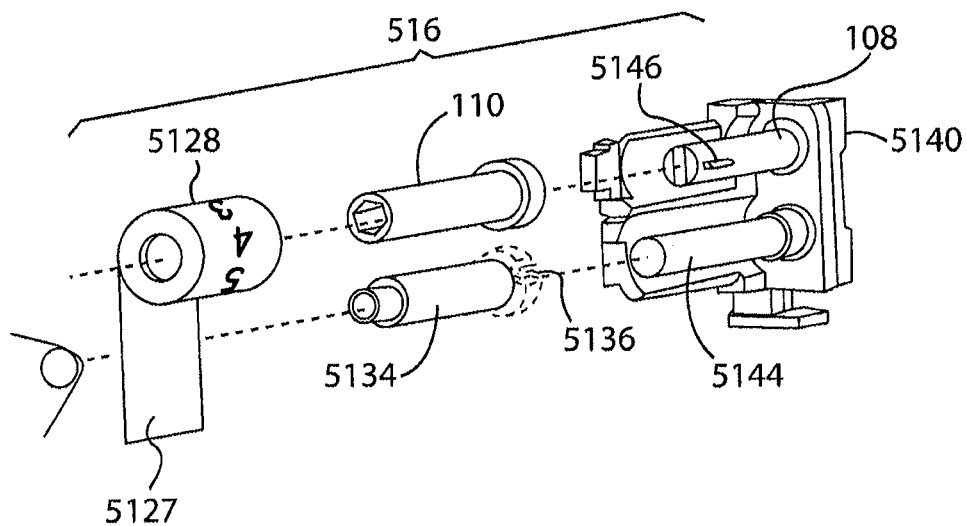


FIG. 24

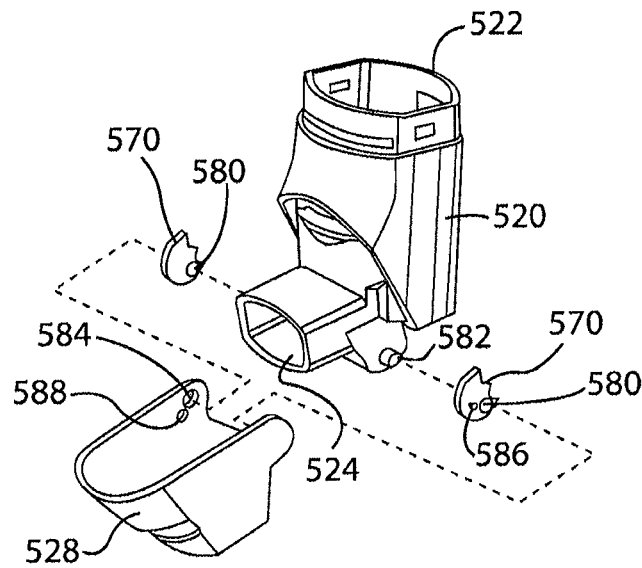


FIG. 25

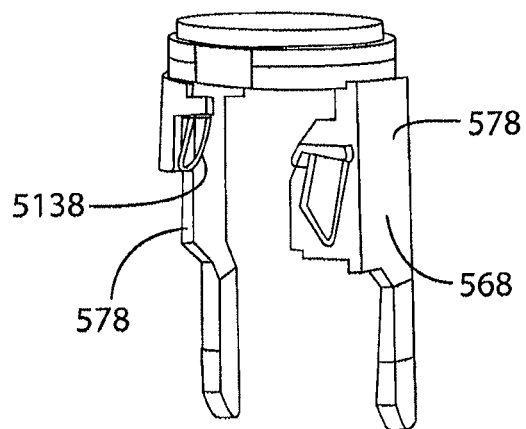


FIG. 26

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DOSE COUNTER FOR INHALER HAVING AN ANTI-REVERSE ROTATION ACTUATOR

CROSS-REFERENCE TO RELATED APPLICATIONS

This patent application is a continuation patent application of U.S. patent application Ser. No. 15/269,249, filed Sep. 19, 2016, now U.S. Pat. No. 9,808,587, which is a continuation of U.S. patent application Ser. No. 14/103,324, filed Dec. 11, 2013, now U.S. Pat. No. 9,463,289, which is a divisional patent application of U.S. patent application Ser. No. 13/110,532, filed May 18, 2011, now U.S. Pat. No. 8,978,966, which claims priority to U.S. patent application No. 61/345,763, filed May 18, 2010, and U.S. patent application No. 61/417,659, filed Nov. 29, 2010, each of which is incorporated herein by reference in its entirety for any and all purposes.

FIELD OF THE INVENTION

The present invention relates to dose counters for inhalers, inhalers and methods of assembly thereof. The invention is particularly applicable to metered dose inhalers including dry power medicament inhalers, breath actuated inhalers and manually operated metered dose medicament inhalers.

BACKGROUND OF THE INVENTION

Metered dose inhalers can comprise a medicament-containing pressurised canister containing a mixture of active drug and propellant. Such canisters are usually formed from a deep-drawn aluminium cup having a crimped lid which carries a metering valve assembly. The metering valve assembly is provided with a protruding valve stem which, in use is inserted as a push fit into a stem block in an actuator body of an inhaler having a drug delivery outlet. In order to actuate a manually operable inhaler, the user applies by hand a compressive force to a closed end of the canister and the internal components of the metering valve assembly are spring loaded so that a compressive force of approximately 15 to 30N is required to activate the device in some typical circumstances.

In response to this compressive force the canister moves axially with respect to the valve stem and the axial movement is sufficient to actuate the metering valve and cause a metered quantity of the drug and the propellant to be expelled through the valve stem. This is then released into a mouthpiece of the inhaler via a nozzle in the stem block, such that a user inhaling through the outlet of the inhaler will receive a dose of the drug.

A drawback of self-administration from an inhaler is that it is difficult to determine how much active drug and/or propellant are left in the inhaler, if any, especially of the active drug and this is potentially hazardous for the user since dosing becomes unreliable and backup devices not always available.

Inhalers incorporating dose counters have therefore become known.

WO 98/028033 discloses an inhaler having a ratchet mechanism for driving a tape drive dose counter. A shaft onto which tape is wound has a friction clutch or spring for restraining the shaft against reverse rotation.

EP-A-1486227 discloses an inhaler for dry powered medicament having a ratchet mechanism for a tape dose counter which is operated when a mouthpiece of the inhaler is closed. Due to the way in which the mouthpiece is opened

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and closed, and actuation pawl of the device which is mounted on a yoke, travels a known long stroke of consistent length as the mouthpiece is opened and closed.

WO 2008/119552 discloses a metered-dose inhaler which is suitable for breath-operated applications and operates with a known and constant canister stroke length of 3.04 mm+/-0.255 mm. A stock bobbin of the counter, from which a tape is unwound, rotates on a shaft having a split pin intended to hold the stock bobbin taut. However, some dose counters do not keep a particularly reliable count, such as if they are dropped onto a hard surface.

More recently, it has become desirable to improve dose counters further and, in particular, it is felt that it would be useful to provide extremely accurate dose counters for manually-operated canister-type metered dose inhalers. Unfortunately, in these inhalers, it has been found in the course of making the present invention that the stroke length of the canister is to a very large extent controlled on each dose operation by the user, and by hand. Therefore, the stroke length is highly variable and it is found to be extremely difficult to provide a highly reliable dose counter for these applications. The dose counter must not count a dose when the canister has not fired since this might wrongly indicate to the user that a dose has been applied and if done repeatedly the user would throw away the canister or whole device before it is really time to change the device due to the active drug and propellant reaching a set minimum. Additionally, the canister must not fire without the dose counter counting because the user may then apply another dose thinking that the canister has not fired, and if this is done repeatedly the active drug and/or propellant may run out while the user thinks the device is still suitable for use according to the counter. It has also been found to be fairly difficult to assembly some known inhaler devices and the dose counters therefor. Additionally, it is felt desirable to improve upon inhalers by making them easily usable after they have been washed with water.

The present invention aims to alleviate at least to a certain extent one or more of the problems of the prior art.

SUMMARY OF THE INVENTION

According to a first aspect of the present invention there is provided a dose counter for an inhaler, the dose counter having a counter display arranged to indicate dosage information, a drive system arranged to move the counter display incrementally in a first direction from a first station to a second station in response to actuation input, wherein a regulator is provided which is arranged to act upon the counter display at the first station to regulate motion of the counter display at the first station to incremental movements.

The regulator is advantageous in that it helps prevent unwanted motion of the counter display if the counter is dropped.

According to a further aspect of the present invention, the regulator provides a resistance force of greater than 0.1 N against movement of the counter display. According to still a further aspect of the present invention, the resistance force is greater than 0.3 N. According to yet a further aspect of the present invention, the resistance force is from 0.3 to 0.4 N.

Preferably, the counter comprises a tape.

Preferably, the tape has dose counter indicia displayed thereon. The first station may comprise a region of the dose counter where tape is held which is located before a display location, such as a display window, for the counter indicia.

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The first station may comprise a first shaft, the tape being arranged on the first shaft and to unwind therefrom upon movement of the counter display.

The first shaft may be mounted for rotation relative to a substantially rotationally fixed element of the dose counter.

The regulator may comprise at least one projection which is arranged on one of the first shaft and the substantially rotationally fixed element and to engage incrementally with one or more formations on the other of the first shaft and the substantially rotationally fixed element.

At least two said projections may be provided. Exactly two said projections may be provided.

Each projection may comprise a radiused surface.

The at least one projection may be located on the substantially fixed element which may comprise a fixed shaft which is fixed to a main body of the dose counter, the first shaft being rotationally mounted to the fixed shaft.

Preferably, the fixed shaft has at least two resiliently flexible legs (or forks). Each leg may have at least one said projection formed in an outwardly facing direction thereon, said one or more formations being formed on an inwardly facing engagement surface of the first shaft, said at least one projection being arranged to resiliently engage said one or more formations. Preferably, a series of said formations are provided. An even number of said formations may be provided. Eight to twelve of said formations may be provided. In one embodiment, ten said formations are provided.

Each said formation may comprise a concavity formed on an engagement surface. Each concavity may comprise a radiused surface wall portion which preferably merges on at least one side thereof into a flat wall portion surface. The engagement surface may include a series of said concavities, and convex wall portions of the engagement surface may be formed between each adjacent two said concavities, each said convex wall portion comprising a convex radiused wall portion.

Each convex radiused wall portion of each convex wall portion may be connected by said flat wall portion surfaces to each adjacent concavity.

The fixed shaft may comprise a split pin with fork legs and each projection may be located on a said fork leg.

The first shaft may comprise a substantially hollow bobbin.

Said at least one formation may be located on an inner surface of the bobbin. In other embodiments it may be located on an outer surface thereof. Said engagement surface may extend partially along said bobbin, a remainder of the respective inner or outer surface having a generally smooth journal portion along at least a portion thereof.

The drive system may comprise a tooth ratchet wheel arranged to act upon a second shaft which is located at the second station, the second shaft being rotatable to wind the tape onto the second shaft.

The second shaft may be located on a main body of the dose counter spaced from and parallel to the first shaft.

The ratchet wheel may be fixed to the second shaft is arranged to rotate therewith. The ratchet wheel may be secured to an end of the second shaft and aligned coaxially with the second shaft.

The dose counter may include anti-back drive system which is arranged to restrict motion of the second shaft. The anti-back drive system may include a substantially fixed tooth arranged to act upon teeth of the ratchet wheel.

According to a further aspect of the present invention, a dose counter includes an anti-back drive system which is arranged to restrict motion of the second shaft in a tape winding direction.

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According to a further aspect of the present invention there is provided a shaft for holding counter tape in a dose counter for an inhaler, the shaft having an engagement surface including incrementally spaced formations located around a periphery thereof, the formations comprising a series of curved concavities and convex portions.

The shaft may comprise a hollow bobbin.

The engagement surface may be a generally cylindrical inwardly directed surface.

The engagement surface may include a flat surface wall portion joining each concavity and convex wall portion.

Each concavity may comprise a radiused wall portion.

Each convex wall portion may comprise a radiused wall portion.

Said concavities may be regularly spaced around a longitudinal axis of the shaft.

Said convex wall portions may be regularly spaced around a longitudinal axis of the shaft.

In some embodiments there may be from eight to twelve said concavities and/or convex wall portions regularly spaced around a longitudinal axis thereof.

One embodiment includes ten said concavities and/or convex wall portions regularly spaced around a longitudinal axis of the shaft.

According to a further aspect of the present invention there is provided a shaft and counter tape assembly for use in a dose counter for an inhaler, the assembly comprising a rotatable shaft and a counter tape which is wound around the shaft and is adapted to unwind therefrom upon inhaler actuation, the shaft having an engagement surface which includes incrementally spaced formations located around a periphery thereof.

According to a further aspect of the present invention there is provided an inhaler for the inhalation of medication and the like, the inhaler including a dose counter as in the first aspect of the present invention.

A preferred construction consists of a manually operated metered dose inhaler including a dose counter chamber including a dose display tape driven by a ratchet wheel which is driven in turn by an actuator pawl actuated by movement of a canister, the tape unwinding from a stock bobbin during use of the inhaler, a rotation regulator being provided for the stock bobbin and comprising a wavelike engagement surface with concavities which engage against control elements in the form of protrusions on resilient forks of a split pin thereby permitting incremental unwinding of the stock bobbin yet resisting excessive rotation if the inhaler is dropped onto a hard surface.

According to another aspect of the present invention there is provided a dose counter for a metered dose inhaler having a body arranged to retain a medicament canister of predetermined configuration for movement of the canister relative thereto; the dose counter comprising: an incremental counting system for counting doses, the incremental counting system having a main body, an actuator arranged to be driven in response to canister motion and to drive an incremental output member in response to canister motion, the actuator and incremental output member being configured to have predetermined canister fire and count configurations in a canister fire sequence, the canister fire configuration being determined by a position of the actuator relative to a datum at which the canister fires medicament and the count configuration being determined by a position of the actuator relative to the datum at which the incremental count system makes an incremental count, wherein the actuator is

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arranged to reach a position thereof in the count configuration at or after a position thereof in the canister fire configuration.

This arrangement has been found to be highly advantageous since it provides an extremely accurate dose counter which is suitable for use with manually operated metered dose inhalers. It has been found that dose counters with these features have a failure rate of less than 50 failed counts per million full canister activation depressions. It has been found in the course of making the present invention that highly reliable counting can be achieved with the dose counter counting at or soon after the point at which the canister fires. It has been is covered by the present inventors that momentum and motion involved in firing the canister, and in some embodiments a slight reduction in canister back pressure on the user at the time of canister firing, can very reliably result in additional further motion past the count point.

The actuator and incremental counting system may be arranged such that the actuator is displaced less than 1 mm, typically 0.25 to 0.75 mm, more preferably about 0.4 to 0.6 mm, relative to the body between its location in the count and fire configurations, about 0.48 mm being preferred. The canister, which can move substantially in line with the actuator, can reliably move this additional distance so as to achieve very reliable counting.

The incremental count system may comprise a ratchet mechanism and the incremental output member may comprise a ratchet wheel having a plurality of circumferentially spaced teeth arranged to engage the actuator.

The actuator may comprise an actuator pawl arranged to engage on teeth of the ratchet wheel. The actuator pawl may be arranged to be connected to or integral with an actuator pin arranged to engage and be depressed by a medicament canister bottom flange. The actuator pawl may be generally U-shaped having two parallel arms arranged to pull on a central pawl member arranged substantially perpendicular thereto. This provides a very reliable actuator pawl which can reliably pull on the teeth of the ratchet wheel.

The incremental count system may include a tape counter having tape with incremental dose indicia located thereon, the tape being positioned on a tape stock bobbin and being arranged to unwind therefrom.

The actuator and incremental output member may be arranged to provide a start configuration at which the actuator is spaced from the ratchet output member, a reset configuration at which the actuator is brought into engagement with the incremental output member during a canister fire sequence, and an end configuration at which the actuator disengages from the ratchet output during a canister fire sequence.

The actuator may be arranged to be located about 1.5 to 2.0 mm, from its location in the fire configuration, when in the start configuration, about 1.80 mm being preferred.

The actuator may be arranged to be located about 1.0 to 1.2 mm, from its location in the fire configuration, when in the reset configuration, about 1.11 mm being preferred.

The actuator may be arranged to be located about 1.1 to 1.3 mm, from its location in the fire configuration, when in the end configuration, about 1.18 mm being preferred.

These arrangements provide extremely reliable dose counting, especially with manually operated canister type metered dose inhalers.

The main body may include a formation for forcing the actuator to disengage from the incremental output member when the actuator is moved past the end configuration. The formation may comprise a bumped up portion of an other-

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wise generally straight surface against which the actuator engages and along which it is arranged to slide during a canister firing sequence.

The dose counter may include a counter pawl, the counter pawl having a tooth arranged to engage the incremental output member, the tooth and incremental output member being arranged to permit one way only incremental relative motion therebetween. When the incremental output member comprises a ratchet wheel, the tooth can therefore serve as an anti-back drive tooth for the ratchet wheel, thereby permitting only one way motion or rotation thereof.

The counter pawl may be substantially fixedly mounted on the main body of the incremental count system and the counter pawl may be arranged to be capable of repeatedly engaging equi-spaced teeth of the incremental output member in anti-back drive interlock configurations as the counter is operated. The counter pawl may be positioned so that the incremental output member is halfway, or substantially halfway moved from one anti-back drive interlock configuration to the next when the actuator and incremental output member are in the end configuration thereof. This is highly advantageous in that it minimises the risk of double counting or non-counting by the dose counter.

According to a further aspect of the invention there is provided an inhaler comprising a main body arranged to retain a medicament canister of predetermined configuration and a dose counter mounted in the main body.

The inhaler main body may include a canister receiving portion and a separate counter chamber, the dose counter being located within the main body thereof, the incremental output member and actuator thereof inside the counter chamber, the main body of the inhaler having wall surfaces separating the canister-receiving portion and the counter chamber, the wall surfaces being provided with a communication aperture, an actuation member extending through the communication aperture to transmit canister motion to the actuator.

According to a further aspect of the present invention there is a provided an inhaler for metered dose inhalation, the inhaler comprising a main body having a canister housing arranged to retain a medicament canister for motion therein, and a dose counter, the dose counter having an actuation member having at least a portion thereof located in the canister housing for operation by movement of a medicament canister, wherein the canister housing has an inner wall, and a first inner wall canister support formation located directly adjacent the actuation member.

This is highly advantageous in that the first inner wall canister support formation can prevent a canister from rocking too much relative to the main body of the inhaler. Since the canister may operate the actuation member of the dose counter, this substantially improves dose counting and avoids counter errors.

The canister housing may have a longitudinal axis which passes through a central outlet port thereof, the central outlet port being arranged to mate with an outer canister fire stem of a medicament canister, the inner wall canister support formation, the actuation member and the outlet port lying in a common plane coincident with the longitudinal axis. Accordingly, this construction may prevent the canister from rocking towards the position of the dose counter actuation member, thereby minimising errors in counting.

The canister housing may have a further inner canister wall support formation located on the inner wall opposite, or substantially opposite, the actuation member. Accordingly, the canister may be supported against rocking motion away from the actuator member so as to minimise count errors.

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The canister housing may be generally straight and tubular and may have an arrangement in which each said inner wall support formation comprises a rail extending longitudinally along the inner wall.

Each said rail may be stepped, in that it may have a first portion located towards a medicine outlet end or stem block of the canister housing which extends inwardly a first distance from a main surface of the inner wall and a second portion located toward an opposite end of the canister chamber which extends inwardly a second, smaller distance from the main surface of the inner wall. This may therefore enable easy insertion of a canister into the canister housing such that a canister can be lined up gradually in step wise function as it is inserted into the canister housing.

The inhaler may include additional canister support rails which are spaced around an inner periphery of the inner wall of the canister housing and which extend longitudinally therealong.

At least one of the additional rails may extend a constant distance inwardly from the main surface of the inner wall.

At least one of the additional rails may be formed with a similar configuration to the first inner wall canister support formation.

The dose counter may, apart from said at least a portion of the actuation member, be located in a counter chamber separate from the canister housing, the actuation member comprising a pin extending through an aperture in a wall which separates the counter chamber and the canister housing.

According to a further aspect of the present invention there is provided an inhaler for inhaling medicaments having: a body for retaining a medicament store; the body including a dose counter, the dose counter having a moveable actuator and a return spring for the actuator, the return spring having a generally cylindrical and annular end; the body having a support formation therein for supporting said end of the return spring, the support formation comprising a shelf onto which said end is engageable and a recess below the shelf.

This shelf and recess arrangement is highly advantageous since it allows a tool (such as manual or mechanical tweezers) to be used to place the return spring of the actuator onto the shelf with the tool then being withdrawn at least partially via the recess.

The shelf may be U-shaped.

The support formation may include a U-shaped upstanding wall extending around the U-shaped shelf, the shelf and upstanding wall thereby forming a step and riser of a stepped arrangement.

The recess below the shelf may also be U-shaped.

At least one chamfered surface may be provided at an entrance to the shelf. This may assist in inserting the actuator and return spring into position.

A further aspect of the invention provides a method of assembly of an inhaler which includes the step of locating said end of said spring on the shelf with an assembly tool and then withdrawing the assembly tool at least partly via the recess. This assembly method is highly advantageous compared to prior art methods in which spring insertion has been difficult and in which withdrawal of the tool has sometimes accidentally withdrawn the spring again.

The cylindrical and annular end of the spring may be movable in a direction transverse to its cylindrical extent into the shelf while being located thereon.

According to a further aspect of the present invention there is provided an inhaler for inhaling medicament, the inhaler having a body for retaining a medicament store; and

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a dose counter, the dose counter having a moveable actuator and a chassis mounted on the body; the chassis being heat staked in position on the body. This is highly advantageous in that the chassis can be very accurately positioned and held firmly in place, thereby further improving counting accuracy compared to prior art arrangements in which some movement of the chassis relative to the body may be tolerated in snap-fit connections.

The chassis may have at least one of a pin or aperture heat staked to a respective aperture or pin of the body.

The chassis may have a ratchet counter output member mounted thereon.

The ratchet counter output member may comprise a ratchet wheel arranged to reel in incrementally a dose meter tape having a dosage indicia located thereon.

According to a further aspect of the present invention there is provided a method of assembling an inhaler including the step of heat staking the chassis onto the body. The step of heat staking is highly advantageous in fixedly positioning the chassis onto the body in order to achieve highly accurate dose counting in the assembled inhaler.

The method of assembly may include mounting a spring-returned ratchet actuator in the body before heat staking the chassis in place. The method of assembly may include pre-assembling the chassis with a dose meter tape prior to the step of heat staking the chassis in place. The method of assembly may include attaching a dose meter cover onto the body after the heat staking step. The cover may be welded onto the body or may in some embodiments be glued or otherwise attached in place.

According to a further aspect of the present invention there is provided an inhaler for inhaling medicament and having a body, the body have a main part thereof for retaining a medicament store; and a dose counter, the dose counter being located in a dose counter chamber of the body which is separated from the main part of the body, the dose counter chamber of the body having a dosage display and being perforated so as to permit the evaporation of water or aqueous matter in the dose counter chamber into the atmosphere.

This is high advantageous since it enables the inhaler to be thoroughly washed and the dose counting chamber can thereafter dry out fully.

The display may comprise a mechanical counter display inside the dose counter chamber and a window for viewing the mechanical counter display. The mechanical counter display may comprise a tape. The perforated dose counter chamber may therefore enable reliable washing of the inhaler, if desired by the user, and may therefore dry out without the display window misting up.

The dose counter chamber may be perforated by a drain hole formed through an outer hole of the body. The drain hole may be located at a bottom portion of the body of the inhaler, thereby enabling full draining of the inhaler to be encouraged after washing when the inhaler is brought into an upright position.

According to a further aspect of the present invention there is provided a dose counter for an inhaler, the dose counter having a display tape arranged to be incrementally driven from a tape stock bobbin onto an incremental tape take-up drive shaft, the bobbin having an internal bore supported by and for rotation about a support shaft, at least one of the bore and support shaft having a protrusion which is resiliently biased into frictional engagement with the other of the bore and support shaft with longitudinally extending mutual frictional interaction. This arrangement may provide good friction for the bobbin, thereby improving tape counter

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display accuracy and preventing the bobbin from unwinding undesirably for example if the inhaler is accidentally dropped.

The support shaft may be forked and resilient for resiliently biasing the support shaft and bore into frictional engagement.

The support shaft may have two forks, or more in some cases, each having a radially extending protrusion having a friction edge extending therealong parallel to a longitudinal axis of the support shaft for frictionally engaging the bore of the support shaft with longitudinally extending frictional interaction therebetween.

The bore may be a smooth circularly cylindrical or substantially cylindrical bore.

Each of the above inhalers in accordance with aspects of the present invention may have a medicament canister mounted thereto.

The canister may comprise a pressurised metered dose canister having a reciprocally movable stem extending therefrom and movable into a main canister portion thereof for releasing a metered dose of medicament under pressure, for example by operating a metered dose valve inside the canister body. The canister may be operable by pressing by hand on the main canister body.

In cases in which one or more support rails or inner wall support formations are provided, the canister may at all times when within the canister chamber have a clearance of about 0.25 to 0.35 mm from the first inner wall support formation. The clearance may be almost exactly 0.3 mm. This clearance which may apply to the canister body itself or to the canister once a label has been applied, is enough to allow smooth motion of the canister in the inhaler while at the same time preventing substantial rocking of the canister which could result in inaccurate counting by a dose counter of the inhaler, especially when lower face of the canister is arranged to engage an actuator member of the dose counter for counting purposes.

According to a further aspect of the invention, a method of assembling a dose counter for an inhaler comprises the steps of providing a tape with dosing indicia thereon; providing tape positioning indicia on the tape; and stowing the tape while monitoring for the tape positioning indicia with a sensor. The method advantageously permits efficient and accurate stowing of the tape, e.g. by winding.

The dosing indicia may be provided as numbers, the tape positioning indicia may be provided as one or more lines across the tape. The stowing step comprises winding the tape onto a bobbin or shaft, and, optionally, stopping winding when the positioning indicia are in a predetermined position. The tape may be provided with pixelated indicia at a position spaced along the tape from the positioning indicia. The tape may also be provided with a priming dot.

According to a further aspect of the invention, a tape system for a dose counter for an inhaler has a main elongate tape structure, and dosing indicia and tape positioning indicia located on the tape structure. The tape positioning indicia may comprise at least one line extending across the tape structure. The tape system may comprise pixelated indicia located on the tape structure and spaced from the positioning indicia. The tape system may comprise a priming dot located on the tape structure. The positioning indicia may be located between the timing dot and the pixelated indicia. The main elongate tape structure may have at least one end thereof wound on a bobbin or shaft.

A further aspect of the invention provides a method of designing an incremental dose counter for an inhaler comprising the steps of calculating nominal canister fire and

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dose counter positions for a dose counter actuator of the inhaler; calculating a failure/success rate for dose counters built to tolerance levels for counting each fire of inhalers in which the dose counter actuators may be applied; and selecting a tolerance level to result in said failure/success rate to be at or below/above a predetermined value. This is highly advantageous in that it allows an efficient and accurate prediction of the reliability of a series of inhaler counters made in accordance with the design.

The method of designing may include selecting the failure/success rate as a failure rate of no more than one in 50 million. The method of designing may include setting an average count position for dose counters built to the tolerances to be at or after an average fire position thereof during canister firing motion. The method of designing may include setting the average count position to be about 0.4 to 0.6 mm after the average fire position, such as about 0.48 mm after. The method of designing may include setting tolerances for the standard deviation of the fire position in dose counters built to the tolerances to be about 0.12 to 0.16 mm, such as about 0.141 mm. The method of designing may include setting tolerances for the standard deviation of the count positions in dose counters built to the tolerances to be about 0.07 to 0.09 mm, such as about 0.08 mm. A further aspect of the invention provides a computer implemented method of designing an incremental dose counter for an inhaler which includes the aforementioned method of designing.

A further aspect of the invention provides a method of manufacturing in a production run a series of incremental dose counters for inhalers which comprises manufacturing the series of dose counters in accordance with the aforementioned method of designing.

A further aspect of the invention provides a method of manufacturing a series of incremental dose counters for inhalers, which comprises manufacturing the dose counters with nominal canister fire and dose count positions of a dose counter actuator relative to a dose counter chassis (or inhaler main body), and which includes building the dose counters with the average dose count position in the series being, in canister fire process, at or after the average canister fire position in the series.

According to a further aspect of the invention, the method provides fitting each dose counter in the series of incremental dose counters to a corresponding main body of an inhaler.

These aspects advantageously provide for the production run of a series of inhalers and dose counters which count reliably in operation.

According to a further aspect of the invention, an incremental dose counter for a metered dose inhaler has a body arranged to retain a canister for movement of the canister relative thereto, the incremental dose counter having a main body, an actuator arranged to be driven and to drive an incremental output member in a count direction in response to canister motion, the actuator being configured to restrict motion of the output member in a direction opposite to the count direction. This advantageously enables an inhaler dose counter to keep a reliable count of remaining doses even if dropped or otherwise jolted.

The output member may comprise a ratchet wheel. The actuator may comprise a pawl and in which the ratchet wheel and pawl are arranged to permit only one-way ratcheting motion of the wheel relative to the pawl. The dose counter may include an anti-back drive member fixed to the main body. In a rest position of the dose counter, the ratchet wheel is capable of adopting a configuration in which a back surface of one tooth thereof engages the anti-back drive member and the pawl is spaced from an adjacent back

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surface of another tooth of the ratchet wheel without positive drive/blocking engagement between the pawl and wheel.

BRIEF DESCRIPTION OF THE DRAWINGS

The present invention may be carried out in various ways and preferred embodiment of a dose counter, inhaler and methods of assembly, design and manufacture will now be described with reference to the accompanying drawings in which:

FIG. 1 is an isometric view of a main body of an embodiment of an inhaler related to the invention together with a mouthpiece cap therefor;

FIG. 2 is a top plan view of the components as shown in FIG. 1;

FIG. 3A is a section on the plane 3A-3A in FIG. 2;

FIG. 3B is a view corresponding to FIG. 3A but with a dose counter fitted to the main body of the inhaler;

FIG. 4A is an exploded view of the inhaler main body, mouthpiece cap, dose counter and a dose counter window;

FIG. 4B is a view in the direction 4B in FIG. 4C of a spring retainer of the dose counter;

FIG. 4C is a top view of the spring retainer of FIG. 4B;

FIG. 5 is a bottom view of the assembled inhaler main body, mouthpiece cap, dose counter and dose counter window;

FIGS. 6A, 6B, 6C, 6D, 6E, 6F, 6G and 6H are various views of dose counter components of the inhaler;

FIGS. 7A and 7B are sectional views showing canister clearance inside the main body of the inhaler;

FIG. 7C is a further sectional view similar to that of FIG. 7B but with the canister removed;

FIG. 7D is a top plan view of the inhaler main body;

FIGS. 8A, 8B, 8C and 8D show the inhaler main body and dose counter components during assembly thereof;

FIG. 9 shows a sectional side view of a datum line for an actuator pawl of the dose counter;

FIGS. 10A, 10B, 10C, 10D, 10E and 10F show various side views of positions and configurations of the actuator pawl, a ratchet wheel, and a count pawl;

FIG. 11 shows distributions for tolerances of start, reset, fire, count and end positions for the actuator of the dose counter;

FIG. 12 is an enlarged version of part of FIG. 4A;

FIG. 13 shows an end portion of a tape of the dose counter;

FIG. 14 shows a computer system for designing the dose counter;

FIG. 15 is an isometric view of a stock bobbin modified in accordance with the present invention for use in the dose counter of the inhaler of FIGS. 1 to 14;

FIG. 16 shows an end view of the stock bobbin of FIG. 15;

FIG. 17 is a section through a longitudinal axis of the stock bobbin of FIGS. 15 and 16;

FIGS. 18A, 18B and 18C are views of the stock bobbin of FIGS. 15 to 17 mounted in the dose counter chassis of FIGS. 1 to 14, with the control elements of the forks of the second shaft (or split pin) having a profile slightly different to that in FIG. 6F, with the forks in a compressed configuration;

FIGS. 19A, 19B and 19C are views equivalent to FIGS. 18A to 18C but with the forks in a more expanded configuration due to a different rotational position of the stock bobbin;

FIG. 20 is an isometric view of the chassis assembled and including the stock bobbin of FIGS. 15 to 17 but excluding the tape for reasons of clarity;

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FIG. 21 is a view of a preferred embodiment of a dry powder inhaler in accordance with the present invention;

FIG. 22 is an exploded view of the inhaler of FIG. 21;

FIG. 23 is a view of a dose counter of the inhaler of FIG. 21;

FIG. 24 is an exploded view of the dose counter shown in FIG. 23;

FIG. 25 is an exploded view of parts of the inhaler of FIG. 21; and

FIG. 26 is a view of a yoke of the inhaler of FIG. 21.

DETAILED DESCRIPTION OF THE INVENTION

FIG. 1 shows a main body 10 of a manually operated metered dose inhaler 12 in accordance with an embodiment related to the present invention and having a mouthpiece cap 14 securable over a mouthpiece 16 of the main body.

The main body has a canister chamber 18 into which a canister 20 (FIG. 7A) is slideable. The canister 20 has a generally cylindrical main side wall 24, joined by a tapered section 26 to a head portion 28 having a substantially flat lower face 30 which has an outer annular drive surface 32 arranged to engage upon and drive an actuation pin 34 of a dose counter 36 as will be described. Extending centrally and axially from the lower face 30 is a valve stem 38 which is arranged to sealingly engage in a valve stem block 40 of the main body 10 of the inhaler 12. The valve stem block 40 has a passageway 42 leading to a nozzle 44 for directing the contents of the canister 20, namely active drug and propellant, towards an air outlet 46 of the inhaler main body 12. It will be appreciated that due to gaps 48 between the canister 20 and an inner wall 50 of the main body 10 of the inhaler 12 an open top 52 of the main body 10 forms an air inlet into the inhaler 12 communicating via air passageway 54 with the air outlet 46, such that canister contents exiting nozzle 44 mix with air being sucked by the user through the air passageway 54 in order to pass together through the air outlet and into the mouth of the user (not shown).

The dose counter 36 will now be described. The dose counter 36 includes an actuation pin 34 biased upwardly from underneath by a return spring 56 once installed in the main body 10. As best shown in FIGS. 4A, 6H and 8A, the pin 34 has side surfaces 58, 60 arranged to slide between corresponding guide surfaces 62, 64 located in a dose counter chamber 66 of the main body 10, as well as an end stop surface 68 arranged to engage a corresponding end stop 70 formed in the dose counter chamber 66 to limit upward movement of the pin 34. The pin 34 has a top part 72 which is circularly cylindrical and extends through an aperture 74 formed through a separator wall 76 which separates the canister chamber 18 from the dose counter chamber 66. The top part 72 of the pin 34 has a flat top surface 78 which is arranged to engage the outer annular drive surface 32 of the canister 20.

The actuation pin 34 is integrally formed with a drive or actuator pawl 80. The actuator pawl 80 has a generally inverted U-shape configuration, having two mutually spaced and parallel arms 82, 84 extending from a base portion of the actuation pin 34, each holding at respective distal ends 88 thereof opposite ends of a pawl tooth member 90 which extends in a direction substantially perpendicular to the arms 82, 84, so as to provide what may be considered a "saddle" drive for pulling on each of the 11 drive teeth 92 of a ratchet wheel 94 of an incremental drive system 96 or ratchet mechanism 96 of the dose counter 36. As shown for example in FIG. 10B, the pawl tooth member 90 has a sharp lower

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longitudinal side edge 98 arranged to engage the drive teeth 92, the edge-to-surface contact provided by this engagement providing very accurate positioning of the actuator pawl 80 and resultant rotational positioning of the ratchet wheel 94.

The dose counter 36 also has a chassis preassembly 100 which, as shown in FIGS. 4A and 6A, includes a chassis 102 having a first shaft 104 receiving the ratchet wheel 94 which is secured to a tape reel shaft 106, and a second shaft (or split pin) 108 which is parallel to and spaced from the first shaft 104 and which slidably and rotationally receives a tape stock bobbin 110.

As shown in FIG. 6B, when the inhaler has not been used at all, the majority of a tape 112 is wound on the tape stock bobbin 110 and the tape 112 has a series of regularly spaced numbers 114 displayed therealong to indicate a number of remaining doses in the canister 20. As the inhaler is repeatedly used, the ratchet wheel 94 is rotated by the actuator pawl 80 due to operation of the actuation pin 34 by the canister 20 and the tape 112 is incrementally and gradually wound on to the tape reel shaft 106 from the second shaft 108. The tape 112 passes around a tape guide 116 of the chassis 102 enabling the numbers 114 to be displayed via a window 118 in a dose counter chamber cover 120 having a dose marker 132 formed or otherwise located thereon.

As shown in FIGS. 6A and 6D, the second shaft 108 is forked with two forks 124, 126. The forks 124, 126 are biased away from one another. The forks have located thereon at diametrically opposed positions on the second shaft 108 friction or control elements 128, 130, one on each fork. Each control element extends longitudinally along its respective fork 124, 126 and has a longitudinally extending friction surface 132, 134 which extends substantially parallel to a longitudinal axis of the second shaft and is adapted to engage inside a substantially cylindrical bore 136 inside the tape stock bobbin 110. This control arrangement provided between the bore 136 and the control elements 128, 130 provides good rotational control for the tape stock bobbin 110 such that it does not unwind undesirably such as when the inhaler is dropped. The tape force required to unwind the tape stock bobbin 110 and overcome this friction force is approximately 0.1 N.

As can be seen in FIG. 6D, as well as FIGS. 6G and 10A to 10F, the chassis 102 is provided with an anti-back drive tooth 138 or count pawl 138 which is resiliently and substantially fixedly mounted thereto. As will be described below and as can be seen in FIGS. 10A to 10F, when the actuation pin 34 is depressed fully so as to fire the metered valve (not shown) inside the canister 20, the actuator pawl 80 pulls down on one of the teeth 92 of the ratchet wheel 94 and rotates the wheel 94 anticlockwise as shown in FIG. 6D so as to jump one tooth 92 past the count pawl 138, thereby winding the tape 112 a distance incrementally relative to the dose marker 122 on the dose counter chamber 120 so as to indicate that one dose has been used.

With reference to FIG. 10B, the teeth of the ratchet wheel 94 have tips 143 which are radiused with a 0.1 mm radius between the flat surfaces 140, 142. The ratchet wheel 94 has a central axis 145 which is 0.11 mm above datum plane 220 (FIG. 9). A top/nose surface 147 of the anti-back drive tooth 138 is located 0.36 mm above the datum plane 220. The distance vertically (i.e. transverse to datum plane 220—FIG. 9) between the top nose surface 147 of the anti-back drive tooth is 0.25 mm from the central axis 145 of the wheel 94. Bump surface 144 has a lateral extent of 0.20 mm, with a vertical length of a flat 145' thereof being 1 mm, the width of the bump surface being 1.22 mm (in the direction of the axis 145), the top 149 of the bump surface 144 being 3.02

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mm vertically below the axis 145, and the flat 145' being spaced a distance sideways (i.e. parallel to the datum plane 220) 2.48 mm from the axis 145. The top surface 78 of the pin 34 (FIG. 6H) is 11.20 mm above the datum plane 220 (FIG. 9) when the actuator pawl 80 and pin 34 are in the start configuration. The length of the valve stem 22 is 11.39 mm and the drive surface 32 of the canister 20 is 11.39 mm above the datum plane 220 when the canister is at rest waiting to be actuated, such that there is a clearance of 0.19 mm between the canister 20 and the pin 34 in this configuration.

FIGS. 10A and 10B show the actuator pawl 80 and ratchet wheel 94 and count pawl 138 in a start position in which the flat top 78 of the pin 34 has not yet been engaged by the outer annular drive surface 32 of the canister 20 or at least has not been pushed down during a canister depression.

In this "start" position, the count pawl 138 engages on a non-return back surface 140 of one of the teeth 92 of the ratchet wheel 94. The lower side edge 98 of the actuator pawl is a distance "D" (FIG. 9) 1.33 mm above datum plane 220 which passes through bottom surface or shoulder 41 of valve stem block 40, the datum plane 220 being perpendicular to a main axis "X" of the main body 10 of the inhaler 12 which is coaxial with the centre of the valve stem block bore 43 and parallel to a direction of sliding of the canister 20 in the main body 10 of the inhaler 12 when the canister is fired.

As shown in FIG. 10B, an advantageous feature of the construction is that the pawl tooth/actuator 90 acts as a supplementary anti-back drive member when the inhaler 12 is not being used for inhalation. In particular, if the inhaler 12 is accidentally dropped, resulting in a jolt to the dose counter 36 then, if the wheel 94 would try to rotate clockwise (backwards) as shown in FIG. 10B, the back surface 140 of a tooth will engage and be blocked by the tooth member 90 of the pawl 80. Therefore, even if the anti-back drive tooth 138 is temporarily bent or overcome by such a jolt, undesirable backwards rotation of the wheel 94 is prevented and, upon the next canister firing sequence, the pawl 90 will force the wheel 94 to catch up to its correct position so that the dose counter 36 continues to provide correct dosage indication.

FIG. 10C shows a configuration in which the actuator pawl 80 has been depressed with the pin 34 by the canister 20 to a position in which the side edge 98 of the pawl tooth member 90 is just engaged with one of the teeth 92 and will therefore upon any further depression of the pin 34 begin to rotate the wheel 94. This is referred to as a "Reset" position or configuration. In this configuration, the lower side edge 98 of the actuator 80 is 0.64 mm above the datum plane 220.

FIG. 10D shows a configuration in which the actuator pawl 80 has been moved to a position lower than that shown in FIG. 10C and in which the metered dose valve (not shown) inside the canister has at this very position fired in order to eject active drug and propellant through the nozzle 44. It will be noted that in this configuration the count pawl 138 is very slightly spaced from the back surface 140 of the same tooth 92 that it was engaging in the configuration of FIG. 10D. The configuration shown in FIG. 10D is known as a "Fire" configuration. In this configuration the lower side edge 98 of the actuator 80 is 0.47 mm below the datum plane 220.

FIG. 10E shows a further step in the sequence, called a "Count" position in which the actuator pawl 80 has rotated the ratchet wheel 94 by the distance circumferentially angularly between two of the teeth 92, such that the count pawl 138 has just finished riding along a forward surface 142 of one of the teeth 92 and has resiliently jumped over the tooth

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into engagement with the back surface **140** of the next tooth. Accordingly, in this "Count" configuration, a sufficiently long stroke movement of the pin **34** has occurred that the tape **112** of the dose counter **36** will just have counted down one dose. In this configuration, the lower side edge **98** of the actuator is 0.95 mm below the datum plane **220**. Accordingly, in this position, the actuator **80** generally, including edge **98**, is 0.48 mm lower than in the fire configuration. It has been found that, although the count configuration happens further on than the fire configuration, counting is highly reliable, with less than 50 failed counts per million. This is at least partially due to momentum effects and to the canister releasing some back pressure on the user in some embodiments as its internal metering valve fires.

In the configuration of FIG. **10F**, the pawl **80** has been further depressed with the pin **34** by the canister **20** to a position in which it is just disengaging from one of the teeth **92** and the actuator pawl **80** is assisted in this disengagement by engagement of one of the arms **84** with a bump surface **144** on the chassis **102** (see FIG. **6G**) and it will be seen at this point of disengagement, which is called an "End" configuration, the count pawl **138** is positioned exactly halfway or substantially halfway between two of the drive teeth **92**. This advantageously means therefore that there is a minimum chance of any double counting or non-counting, which would be undesirable. In the end configuration, the side edge **98** of the actuator is 1.65 mm below the datum plane **220**. It will be appreciated that any further depression of the actuator pawl **80** and pin **34** past the "End" configuration shown in FIG. **10F** will have no effect on the position of the tape **112** displayed by the dose counter **36** since the actuator pawl **80** is disengaged from the ratchet wheel **94** when it is below the position shown in FIG. **10F**.

As shown in FIGS. **7C** and **7D**, the inner wall **50** of the main body **10** is provided with a two-step support rail **144** which extends longitudinally along inside the main body and is located directly adjacent the aperture **74**. As shown in FIG. **7B** a diametrically opposed two-step support rail **146** is also provided and this diametrically opposed in the sense that a vertical plane (not shown) can pass substantially directly through the first rail **144**, the aperture **74**, a central aperture **148** of the valve stem block **40** (in which canister stem **25** is located) and the second two-step support rail **146**. As shown in FIG. **7A** and schematically in FIG. **7B**, the rails **144**, **146** provide a maximum clearance between the canister **20** and the rails **144**, **146** in a radial direction of almost exactly 0.3 mm, about 0.25 to 0.35 mm being a typical range. This clearance in this plane means that the canister **20** can only rock backwards and forwards in this plane towards away from the actuation pin **34**. A relatively small distance and this therefore prevents the canister wobbling and changing the height of the actuation pin **34** as to undesirably alter the accuracy of the dose counter **36**. This is therefore highly advantageous.

The inner wall **50** of the main body **10** is provided with two further two-step rails **150** as well as two pairs **152**, **154** of rails extending different constant radial amounts inwardly from the inner wall **50**, so as to generally achieve a maximum clearance of almost exactly 0.3 mm around the canister **20** for all of the rails **144**, **146**, **150**, **152**, **154** spaced around the periphery of the inner wall **50**, in order to prevent undue rocking while still allowing canister motion freely inside the inhaler **12**. It will be clear from FIG. **7C** for example that the two-step rails have a first portion near an outlet end **156** of the canister chamber **18**, the first portion having a substantially constant radial or inwardly-extending width, a first step **160** leading to a second portion **162** of the rail, the

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second portion **102** having a lesser radial or inwardly extending extent than the first portion **156**, and finally a second step **164** at which the rail merges into the main inner wall **50** main surface.

A method of assembling the inhaler **12** will now be described.

With reference to FIG. **8A**, the main body **10** of the inhaler **12** is formed by two or more plastics mouldings which have been joined together to the configuration shown.

As shown in FIG. **8B**, the actuator pawl **80** and pin **34** are translated forward into position into a pin receiving area **166** in the dose counter chamber **66** and the pin **34** and actuator **80** may then be raised until the pin **34** emerges through the aperture **74**.

Next, the return spring **56** may be inserted below the pin **34** and a generally cylindrical annular lower end **168** of the spring **56** may be moved by a tweezer or tweezer-like assembly tool (not shown) into engagement with a shelf **170** of a spring retainer **172** in the dose counter chamber **66**. The spring retainer **172** is U-shaped and the shelf **170** is U-shaped and has a recess **174** formed below it. As shown in FIGS. **4B**, **4C** and **12** shelf **170** includes three chamfer surfaces **176**, **178**, **180** arranged to assist in moving the lower end of the spring **168** into position onto the shelf using the assembly tool (not shown). Once the lower end of the spring **168** is in place, the assembly tool (not shown) can easily be removed at least partly via the recess **174** below the lower end **168** of the spring **56**.

The tape **112** is attached at one end (not shown) to the tape stock bobbin **110** and is wound onto the bobbin by a motor **200** (FIG. **13**) having a hexagonal output shaft **202** which engages in a hexagonal socket **204** (FIG. **6B**) of the bobbin. During winding, the tape is monitored by a sensor **206**, which may be in the form of a camera or laser scanner, which feeds data to a computer controller **205** for the motor **200**. The controller **205** recognises three positioning markers **210** in the form of lines across the tape **112** and stops the motor **202** when the tape **112** is nearly fully wound onto the bobbin **110**, such that the distal end **212** of the tape **112** can be secured, e.g. by adhesive, to the tape reel shaft **106**. The controller **205** also recognises a pixelated tape size marker **214** observed by the sensor **206** and logs in a stocking system data store **217** details of the tape **112** such as the number of numbers **114** on the tape, such as one hundred and twenty or two hundred numbers **114**. Next, the tape reel shaft is wound until an appropriate position of the lines **210** at which a priming dot **216** will, once the bobbin **110** and reel shaft **106** are slid onto the second shaft **108** and second shaft **104**, be in a position to be located in the window **118** when the inhaler **12** is fully assembled. In the embodiments, the bobbin **110** and reel shaft **106** may be slid onto the shafts **108**, **104** before the tape **112** is secured to the reel shaft **106** and the reel shaft may then be wound to position the priming dot **216**.

Next, the assembled dose counter components of the chassis preassembly **100** shown in FIG. **6B** may as shown in FIG. **8C** be inserted into the dose counter chamber **66**, with pins **182**, **184**, **186** formed on the main body **10** in the dose counter chamber **66** passing through apertures or slots **188**, **190**, **192** formed on the chassis **102**, such that the pins **182**, **184**, **186** extend through (or at least into) the apertures or slots **188**, **190**, **192**. With the chassis **102** being relatively firmly pushed towards the main body **10**, the pins **182**, **184**, **186** are then heat staked and the chassis **102** is therefore after this held very firmly in position in the main body and is unable to move, thereby assisting in providing great accuracy for the dose counter **36**. Next, as shown in FIG. **8D**, the

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dose counter chamber cover **120** may be fitted over the dose counter chamber **66** and may be secured in place such as by welding, with the priming dot **216** being displayed through the window.

The user can, when readying the inhaler **12** for first use, prime the inhaler by depressing the canister **20** three times which will bring the first number **114** on the tape into display through the window **118** in place of the priming dot **216**, the number **114** shown in FIG. **8D** being “200”, thereby indicating that 200 doses are remaining to be dispensed from the canister **20** and inhaler **12**.

As shown in FIG. **8D**, and in FIG. **5**, an open drain hole **194** is provided at the bottom of the dose counter chamber **66** by a substantially semi-circular cut-out or recess formation **196** in a lower surface **198** of the main body **10** of the inhaler. Accordingly, if the user (not shown) should decide to wash the main body **10** of the inhaler, for example after encountering an unhygienic situation or simply as a matter of choice, the drain hole **194** allows initial draining of water from inside the dose counter chamber **66** and also thereafter evaporation of water or any aqueous matter in the dose counter chamber **66** so that the window **118** does not mist up undesirably.

FIG. **14** shows a computer system **230** for designing the dose counter **36** and in particular for calculating distributions representative of average positions and standard deviations in a production series of inhalers of the start, reset, fire, count and end positions of the actuator lower side edge **98** relative to the datum plane **220** (FIG. **9**) and therefore of the actuator pawl **80** generally relative to the ratchet wheel **94**, chassis **102** and, when the inhaler **12** is fully assembled, the main body **10** of the inhaler **12**. The computer system **230** includes a data store **232**, a CPU **234**, an input device **236** (such as a keyboard or communication port) and an output device **238** (such as a communications port, display screen and/or printer). A user may enter data via the input device **236** which may be used by the CPU **234** in a mathematical calculation to predict count failure rates when the various dose counters are to be built in a series with dose counter positions set with given averages and standard deviations and taking into account any momentum/inertia effects and metering valve user-back-pressure reduction effect which will occur upon canister firing of a given type of canister. The computer system **230** is thus mathematically used to design the distributions. For the inhaler **12** described herein with the dose counter **36** and canister **20**, the distributions are designed as shown in FIG. **11**. The x axis shows distance of the lower side surface **98** of the actuator **80** above the datum plane **220** and the y axis is representative of the distribution. Thus, curve **240** shows that the start configuration has an average 1.33 mm above the datum plane **200** (standard deviation is 0.1 mm), curve **242** shows that the reset configuration has an average of 0.64 mm above the datum plane **220** (standard deviation is 0.082 mm), curve **244** shows the fire configuration has an average 0.47 mm below the datum plane **220** (standard deviation is 0.141 mm), curve **246** shows the count configuration has an average 0.95 mm below the datum plane **220** (standard deviation is 0.080 mm), and curve **248** shows the end configuration has an average of 1.65 mm below the datum plane **220** (standard deviation is 0.144 mm).

FIGS. **15** to **20** show a version of the inhaler modified in accordance with the present invention. In these drawings, the same reference numerals have been used to those in the earlier drawings to denote the equivalent components. The inhaler **12** is the same as that in FIGS. **1** to **14** apart from the following modifications.

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First, it can be seen that there is a modification in that the drive teeth **92** of the ratchet wheel **94** have a different profile to that in FIGS. **1** to **14**. There are also only nine ratchet teeth **94** in this embodiment instead of eleven.

Additionally, as shown in FIGS. **18C** and **19C**, the control elements **128**, **130** on the forks **124**, **126** of the second shaft **108** have a tapered profile which is different to the profile of the control elements **128**, **130** shown in FIG. **6F**. Either profile can be used in the embodiment of FIGS. **15** to **20** however.

Furthermore, as shown in FIG. **15**, the tape stock bobbin **110** has an inwardly facing generally cylindrical engagement surface **300** with a wavelike form extending partially therealong. The engagement surface **300** has a cross-section **301** perpendicular to the longitudinal length of the stock bobbin **110** which is constant therealong. This cross-section **301** can be seen in FIG. **16** and consists of a series of ten regularly spaced concavities **302** and ten convex wall portions **304**. The convex wall portions **304** are equi-spaced between the concavities **302**. Each concavity **302** has a radius of 0.2 mm. Each convex wall portion **304** also has a radius of 0.2 mm. Finally, the cross section **301** also includes flat wall portions **306** between all of the radiused wall portions of the concavities **302** and convex wall portions **304**. The geometry of the cross-section **301** is therefore defined by the radii of the concavities **302** and convex wall portions **304**, the flat wall portions **306** and the fact that there are ten concavities **302** and convex wall portions **304**.

The minor diameter of the engagement surface **300**, i.e. between the tips of opposite convex wall portions **304**, is 2.46 mm. The major diameter of the engagement surface **300**, i.e. between the outermost portions of the concavities **302**, is 2.70 mm. The undeformed tip to tip maximum diameter of the forks **124**, **126** of the split pin (the second shaft) **108**, i.e. in the region of the maximum radio extent of the control elements **128**, **130**, is 3.1 millimetres and it will therefore be appreciated that the forks **124**, **126** are resiliently compressed once the stock bobbin **110** has been assembled onto the split pin **108** in all rotational configurations of the stock bobbin **110** relative to the split pin **108**. The minimum gap between the forks **124**, **126** in the plane of the cross sections of FIGS. **18C** and **19C** is 1 mm when the split pin **108** is in the undeformed, pre-inserted state. When the split pin **108** is at maximum compression, as shown in FIGS. **18A** to **18C** when the control elements **128**, **130** are shown to be engaged on top of the convex wall portions **304**, the gap **308** between the tips **310**, **312** of the forks **124**, **126** is 0.36 mm. On the other hand, when the split pin **108** is at minimum compression (once inserted into the stock bobbin) as shown in FIGS. **19A** to **19C**, when the control elements **128**, **130** rest in the concavities **302**, the gap between the tips **310**, **312** of the forks **124**, **126** is 0.6 mm. The control elements **128**, **130** are outwardly radiused with a radius also of 0.2 mm such that they can just rest on the concavities **302** with full surface contact (at least at an axial location on the split pin where the tapered control elements are at their maximum radial extent), without rattling in, locking onto or failing to fit in the concavities **302**. The radii of the control elements **128**, **130** is therefore preferably substantially the same as the radii of the concavities **302**.

It will be appreciated that whereas FIGS. **18B** and **19B** are end views along the coaxial axis of the stock bobbin **110** and split pin **108**, FIGS. **18A** and **19A** are cross-sections. FIG. **19A** is a section on the plane A-A' in FIG. **19C** and FIG. **18A** is a section at the same plane, but of course with the stock bobbin **110** rotated relative to the split pin **108**.

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As the inhaler 12 is used and the ratchet wheel 94 rotates in order to count used doses, the stock bobbin rotates incrementally through rotational positions in which rotation is resisted, i.e. due to increasing compression of the split pin 108 at such rotational positions, and rotational positions in which rotation is promoted, i.e. due to decreasing compression of the split pin 108 at such rotational positions and this may involve a click forward of the stock bobbin 110 to the next position equivalent to that in FIGS. 19A to 19C in which the control elements 128, 130 of the split pin art located in the concavities 302. This functionality firstly allows the stock bobbin to unwind during use as required, but also prevents the tape 112 from loosening during transit if the inhaler 12 is dropped, such as onto a hard surface. This is highly advantageous, since the tape 11 is prevented from moving to a position in which it will give an incorrect reading regarding the number of doses in the canister.

During compression and expansion of the forks in the radial direction between the two configurations shown in FIGS. 18C and 19C, the forks 124, 126 rotate about a point 316 on the split pin where the forks 124, 126 come together. This rotational action means that there is a camming action between the forks 124, 126 and the engagement surface 300 without significant friction but, nevertheless, the resilient forces provided by the regulator formed by the engagement surface 300 and forks 124, 126 are able to regulate unwinding of the tape such that it does not easily occur during transit or if the inhaler 12 is dropped. It has been found during testing that a force of 0.3 to 0.4 N needs to be applied to the tape 112 to overcome the regulator at the stock bobbin 110. 0.32 N is achieved with the control elements 128 having the profile shown in FIG. 19C and 0.38 N is achieved with the profile of the control elements 128 altered to be as shown as described with reference to FIG. 6F. These forces are substantially higher than the 0.1 N force mentioned above and undesirable movement of the tape is substantially avoided even if the inhaler is dropped onto a hard surface. The modified arrangement of FIGS. 15 to 20 does not provide this force "constantly" such that there is overall not an undesirably high friction of the tape 112 as it passes over the other components of the dose counter because, due to the incremental nature of the resilient forces at the regulator, the tape 112 can incrementally relax as it slides over the stationary chassis components.

Instead of having ten concavities 302 and convex wall portions 304, other numbers may be used, such as 8 or 12. However, it is preferred to have an even number, especially since two control elements 128, 130 are provided, so that all of the control elements 128, 130 will expand and contract simultaneously. However, other arrangements are envisaged with 3 or more forks and the number of concavities/convex wall portions may be maintained as an integer divisible by the number of forks to maintain a system with simultaneous expansion/contraction. For example, the use of 9, 12 or 15 concavities/convex wall portions with 3 forks is envisaged.

Instead of having the engagement surface 300 on the inside of the stock bobbin 110, it could be placed on the outside of the stock bobbin 110 so as to be engaged by flexible external legs/pawls or similar.

It will be noted that the regulator provided by the engagement surface 300 and forks 124, 126 does not only allow rotation of the stock bobbin in one direction as is the case with the ratchet wheel 94. Rotation in both directions is possible, i.e. forwards and backwards. This means that during assembly, the stock bobbin 110 can be wound backwards during or after fitting the bobbin 100, shaft 106 and tape 112 onto the carriage 102, if desired.

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The stock bobbin 110 and the carriage 102 including the split pin 108 are both moulded of polypropylene material.

It will be seen from FIG. 16 that the cross-sectional shape 301 is not symmetrical within the hexagonal socket 204. This has enabled the hexagonal socket 204 to be maintained at a useful size while still allowing the desired size and geometry of the cross section 301 to fit without interfering with the hexagonal shape of the hexagonal socket 204 and also permits moulding to work during manufacture.

As shown in FIG. 17, the stock bobbin 110 has a series of four circumferential ribs 330 inside it and a spaced therealong. These hold the stock bobbin 110 on the correct side of the mould tool during moulding.

FIGS. 21 and 22 show a preferred embodiment in accordance with the invention of an inhaler 510 for dispensing a dry-powdered medicament in metered doses for patient inhalation. The inhaler 510 is as disclosed in FIGS. 1 to 16 or EP-A-1330280, the contents of which are hereby fully incorporated herein by reference, but with the stock bobbin 110 and second shaft 108 of the dose counter 516 modified so as to be as in FIGS. 15 to 20 hereof. Thus, the dry powder inhaler 510 generally includes a housing 518, and an assembly 512 received in the housing (see FIG. 21). The housing 518 includes a case 520 having an open end 522 and a mouthpiece 524 (FIG. 25) for patient inhalation, a cap 526 secured to and closing the open end 522 of the case 520, and a cover 528 pivotally mounted to the case 520 for covering the mouthpiece 524. As shown in FIG. 22, the inhaler 510 also includes an actuation spring 569, first yoke 566 with opening 572, bellows 540 with crown 574, a reservoir 514, second yoke 568 with hopper 542 and dose counter 516 mounted thereto, and case 520 has transparent window 5130 thereon for viewing dose counter tape indicia 5128. The dose metering system also includes two cams 570 mounted on the mouthpiece cover 528 and movable with the cover 528 between open and closed positions. The cams 570 each include an opening 580 for allowing outwardly extending hinges 582 of the case 520 to pass therethrough and be received in first recesses 584 of the cover 528. The cams 570 also include bosses 586 extending outwardly and received in second recesses 588 of the cover 528, such that the cover 528 pivots about the hinges 582 and the cams 570 move with the cover 528 about the hinges 582. As described in EP-A-1330280, cams 570 act upon cam followers 578 to move second yoke 568 up and down and thereby operate dose counter by engagement of pawl 5138 on the second yoke 568 with teeth 5136. Remaining components of the inhaler are provided as, and operate as described, in EP-A-1330280.

The dose counting system 516 therefore includes a ribbon or tape 5128 (FIGS. 23 & 24), having successive numbers or other suitable indicia printed thereon, in alignment with a transparent window 5130 provided in the housing 18 (see FIG. 22). The dose counting system 516 includes the rotatable stock bobbin 110 (as described above), an indexing spool 5134 rotatable in a single direction, and the ribbon 5128 rolled and received on the bobbin 110 and having a first end 5127 secured to the spool 5134, wherein the ribbon 5128 unrolls from the bobbin 110 so that the indicia are successively displayed as the spool 5134 is rotated or advanced. In FIGS. 23 and 24 the wavelike engagement surface 300 of the bobbin 110 is not shown for the purposes of clarity.

The spool 134 is arranged to rotate upon movement of the yokes 566, 568 to effect delivery of a dose of medicament from reservoir 514, such that the number on the ribbon 5128 is advanced to indicate that another dose has been dispensed by the inhaler 510. The ribbon 5128 can be arranged such that the numbers, or other suitable indicia, increase or

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decrease upon rotation of the spool **5134**. For example, the ribbon **5128** can be arranged such that the numbers, or other suitable indicia, decrease upon rotation of the spool **5134** to indicate the number of doses remaining in the inhaler **510**. Alternatively, the ribbon **5128** can be arranged such that the numbers, or other suitable indicia, increase upon rotation of the spool **5134** to indicate the number of doses dispensed by the inhaler **10**.

The indexing spool **5134** includes radially extending teeth **5136**, which are engaged by pawl **5138** extending from a cam follower **578** of the second yoke **568** upon movement of the yoke to rotate, or advance, the indexing spool **5134**. More particularly, the pawl **5138** is shaped and arranged such that it engages the teeth **5136** and advances the indexing spool **5134** only upon the mouthpiece cover **528** being closed and the yokes **566**, **568** moved back towards the cap **526** of the housing **518**.

The dose counting system **516** also includes a chassis **5140** that secures the dose counting system to the hopper **542** and includes shafts **108**, **5144** for receiving the bobbin **110** and the indexing spool **5134**. As described above with reference to FIGS. **1** to **20**, the bobbin shaft **108** is forked and includes radially nubs **5146** for creating a resilient resistance to rotation of the bobbin **110** on the shaft **108** by engaging with the wavelike engagement surface **300** inside the bobbin **110**. A clutch spring **5148** is received on the end of the indexing spool **5134** and locked to the chassis **5140** to allow rotation of the spool **5134** in only a single direction.

Various modifications may be made to the embodiment shown without departing from the scope of the invention as defined by the accompanying claims as interpreted under patent law.

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What is claimed is:

1. An inhaler for inhaling medicament, the inhaler having: A body for retaining a medicament canister; and a dose counter, the dose counter having a moveable actuator and a chassis mounted on the body; wherein one of the body and the chassis includes a plurality of apertures for receiving one or more pins on the other of the body and the chassis, wherein either the pins or the apertures on the chassis are positioned on different sides of the chassis for stabilizing the chassis on the body, and wherein the chassis comprises at least one of a pin or aperture heat staked to a respective aperture or pin of the body to mount the chassis to the body.
2. The inhaler as claimed in claim **1**, wherein the dose counter is positioned in a dose counter chamber that is formed in the body at a location beneath the medicament canister.
3. The inhaler as claimed in claim **2** further comprising a cover that is fixed to the body to conceal the dose counter chamber.
4. The inhaler as claimed in claim **1**, wherein the medicament canister is movable relative to the dose counter.
5. The inhaler as claimed in claim **1**, wherein the body has a canister housing and the medicament canister is moveable relative to the canister housing, wherein at least a portion of the movable actuator of the dose counter is located in the canister housing for operation by movement of the medicament canister.
6. The inhaler as claimed in claim **1**, wherein either the pins or the apertures on the chassis are positioned on three different sides of the chassis for stabilizing the chassis on the body.

* * * * *

EXHIBIT H

(12) **United States Patent**
Walsh et al.

(10) **Patent No.:** **US 10,792,447 B2**

(45) **Date of Patent:** **Oct. 6, 2020**

(54) **BREATH ACTUATED INHALER**

(56) **References Cited**

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Waterford (IE)

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(72) Inventors: **Declan Walsh**, Waterford (IE); **Paul Prendergast**, Waterford (IE); **Daniel Buck**, Waterford (IE); **Trevor Kent**, Waterford (IE); **Niall Thompson**, Waterford (IE)

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(73) Assignee: **NORTON (WATERFORD) LIMITED**, Waterford (IE)

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(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

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Primary Examiner — Colin W Stuart

Assistant Examiner — Douglas Y Sul

(65) **Prior Publication Data**

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(74) *Attorney, Agent, or Firm* — Morgan, Lewis & Bockius LLP

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(57) **ABSTRACT**

(51) **Int. Cl.**

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CPC **A61M 15/0095** (2014.02); **A61K 31/46** (2013.01); **A61K 31/575** (2013.01);

(Continued)

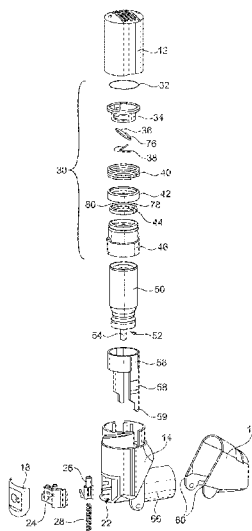
(58) **Field of Classification Search**

CPC A61M 15/0091; A61M 15/0093; A61M 15/0095; A61M 15/0096; A61M 15/009;

(Continued)

A breath actuated metered dose inhaler may include a canister fire system configured to fire a medicament containing canister in response to patient inhalation. The canister fire system may include a pneumatic force holding unit and having a rest configuration in which a metering valve of the canister is in a refill configuration; a prepared configuration in which a canister actuation force is retained by the pneumatic force holding unit and the canister fire system is actuable by patient inhalation induced airflow; and a fire configuration in which the metering valve is in a dose delivery position. When in the prepared configuration, the force retained by the so pneumatic force holding unit may be reduced by less than about 6% over a period of 5 minutes, preferably less than about 3% over a period of 5 minutes.

10 Claims, 9 Drawing Sheets



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(51) **Int. Cl.**

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A61K 31/575 (2006.01)
B29C 45/37 (2006.01)

(52) **U.S. Cl.**

CPC *A61M 15/009* (2013.01); *A61M 16/208*
(2013.01); *A61M 39/24* (2013.01); *A61M*
15/0026 (2014.02); *A61M 15/0068* (2014.02);
A61M 2016/0015 (2013.01); *A61M 2039/242*
(2013.01); *A61M 2039/244* (2013.01); *A61M*
2202/064 (2013.01); *A61M 2207/10* (2013.01);
B29C 45/37 (2013.01); *B29K 2995/0072*
(2013.01); *B29K 2995/0073* (2013.01)

(58) **Field of Classification Search**

CPC A61M 11/08; A61M 16/208; A61M
15/0026; A61M 2207/00; A61M 2207/10;
A61M 2016/0015; A61M 2039/242;
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See application file for complete search history.

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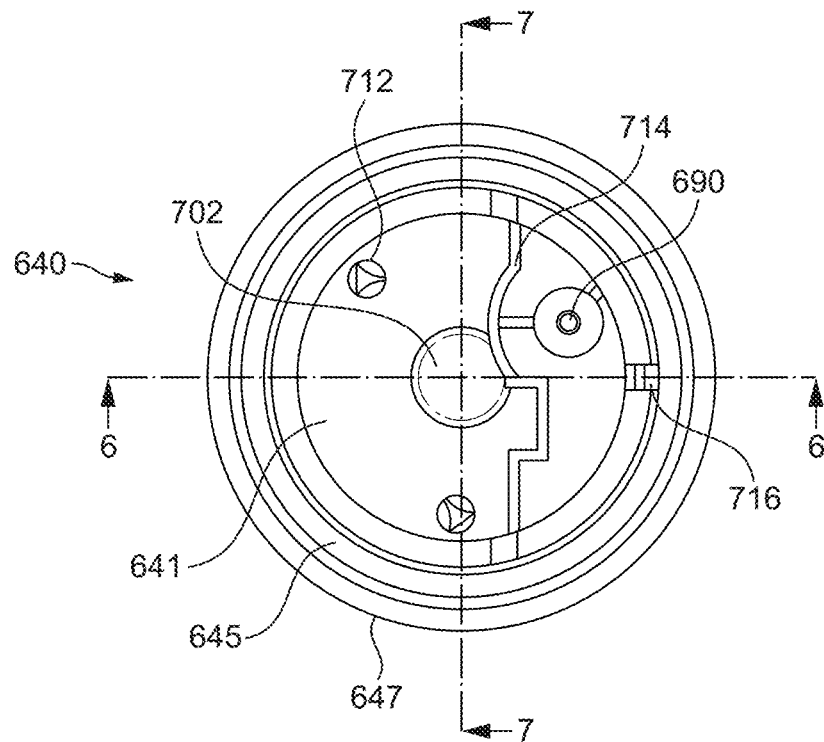


FIG. 1
PRIOR ART

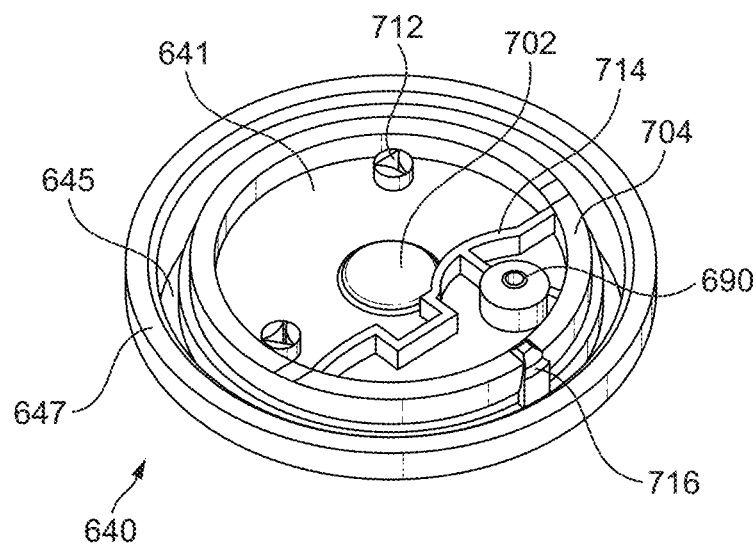
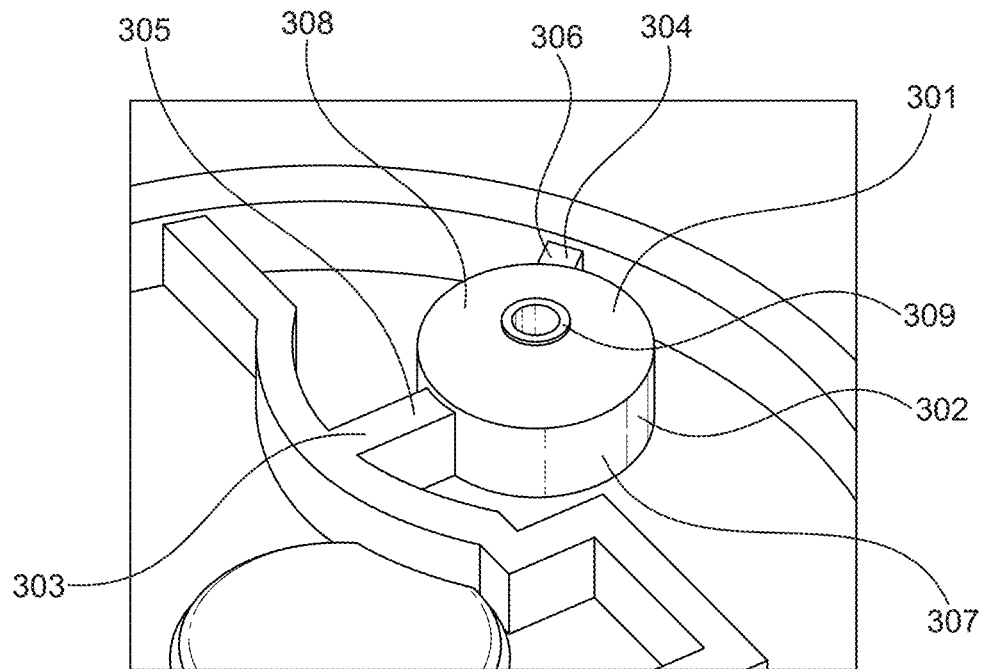


FIG. 2
PRIOR ART



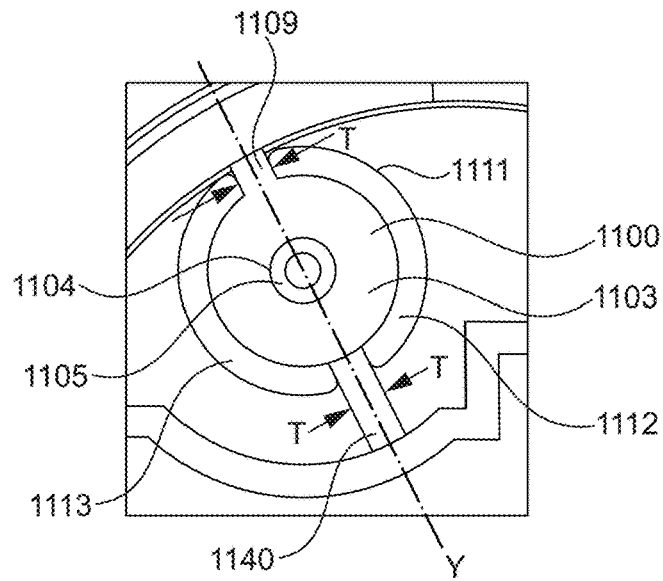


FIG. 5

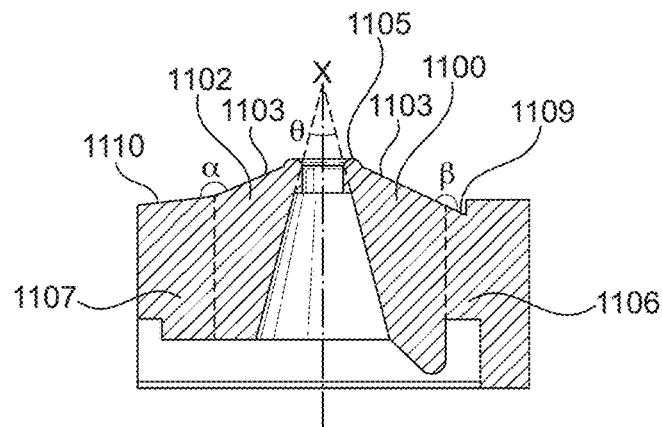


FIG. 6

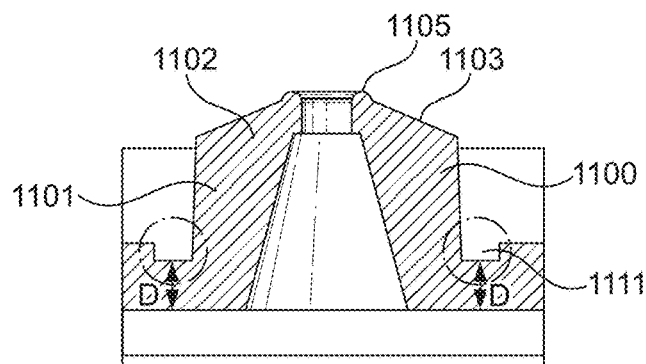


FIG. 7

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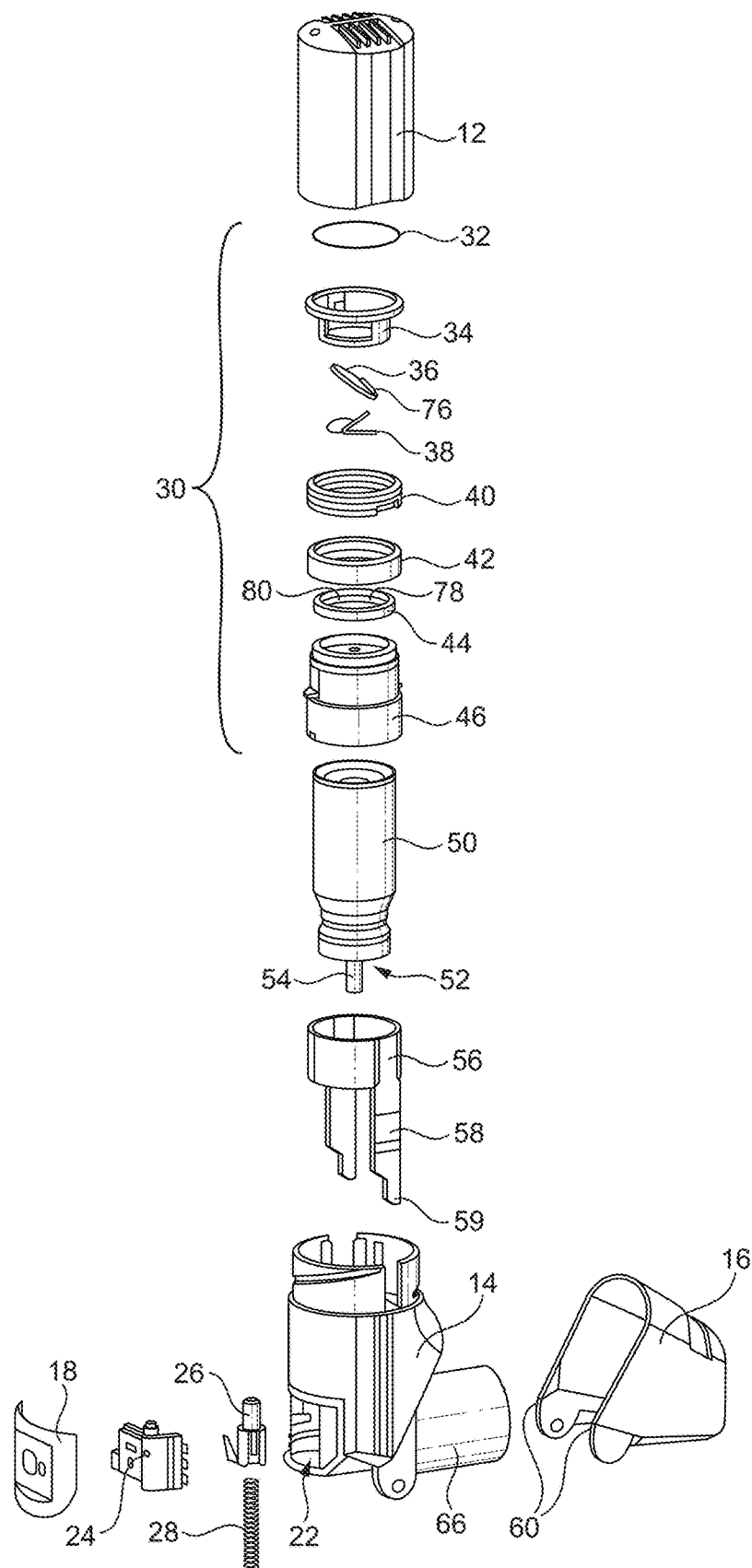


FIG. 8

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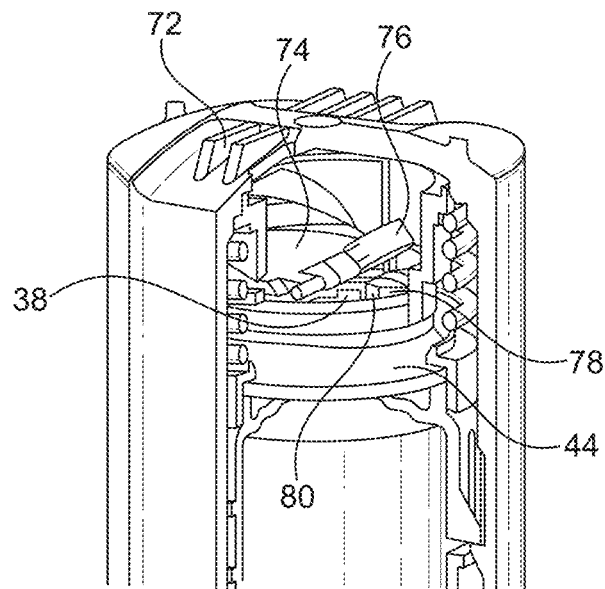


FIG. 9

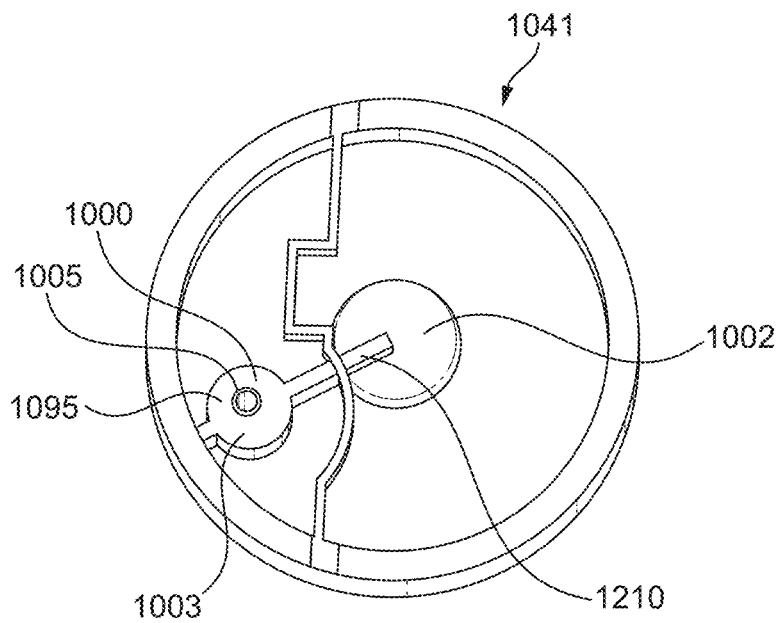


FIG. 10

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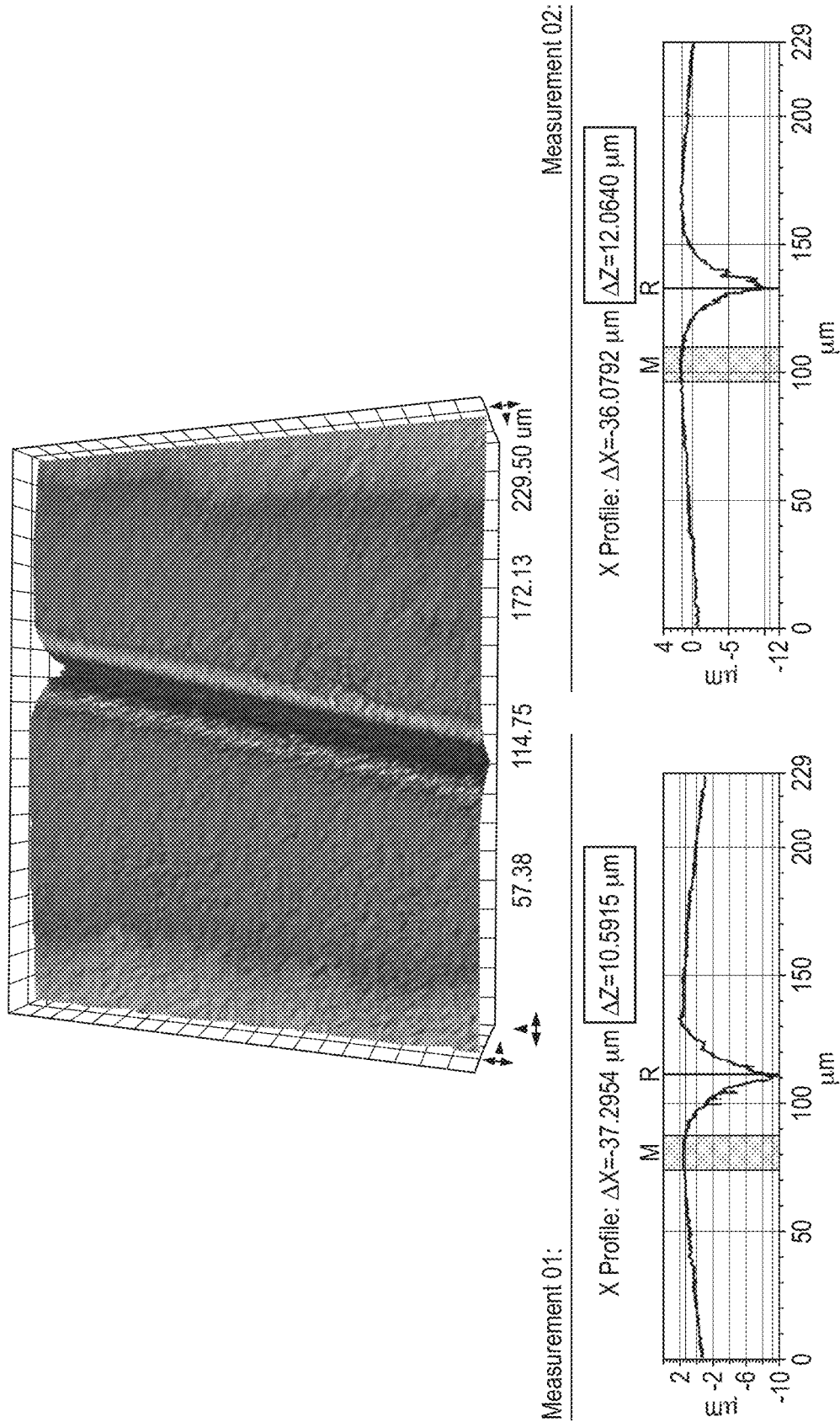


FIG. 11

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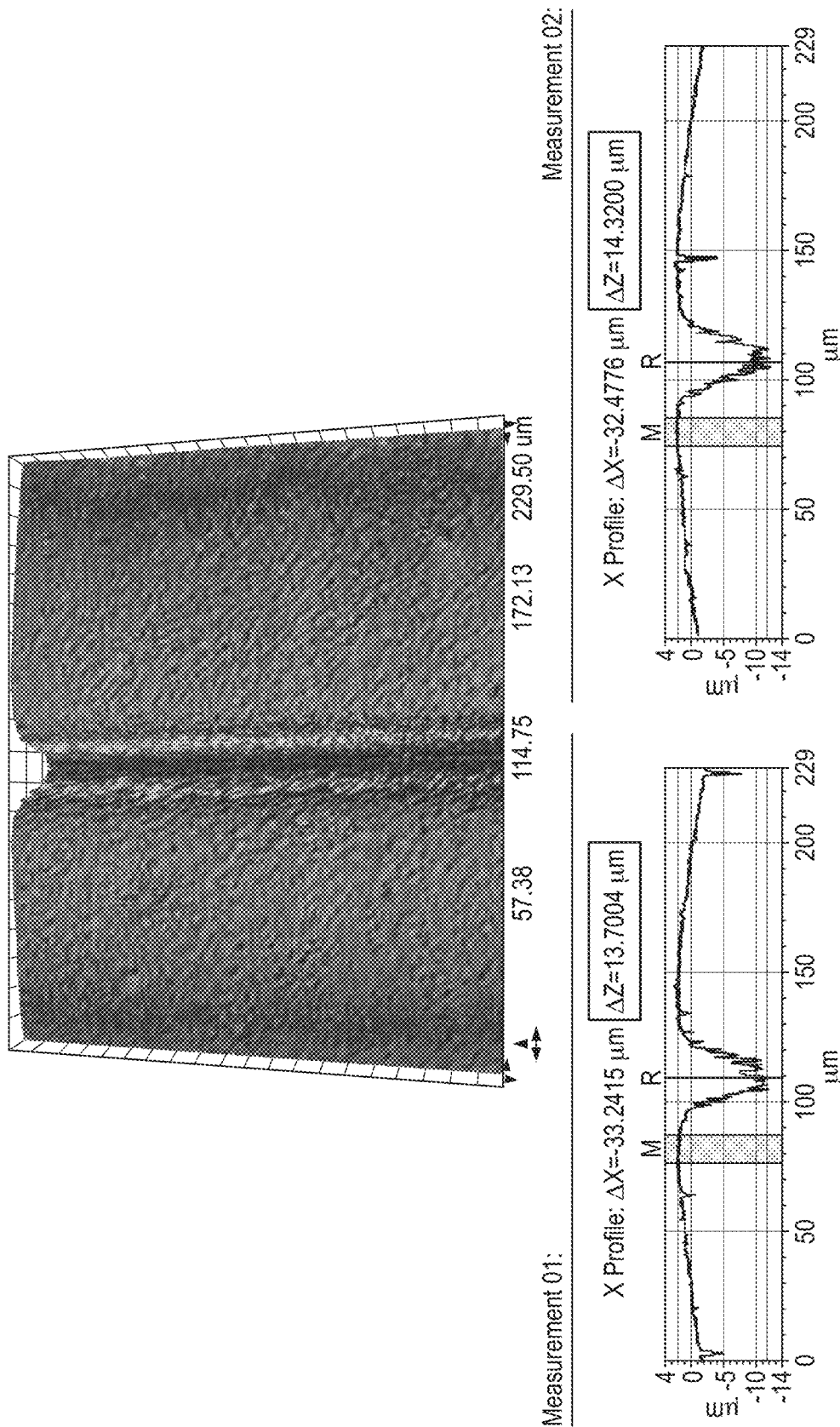


FIG. 12

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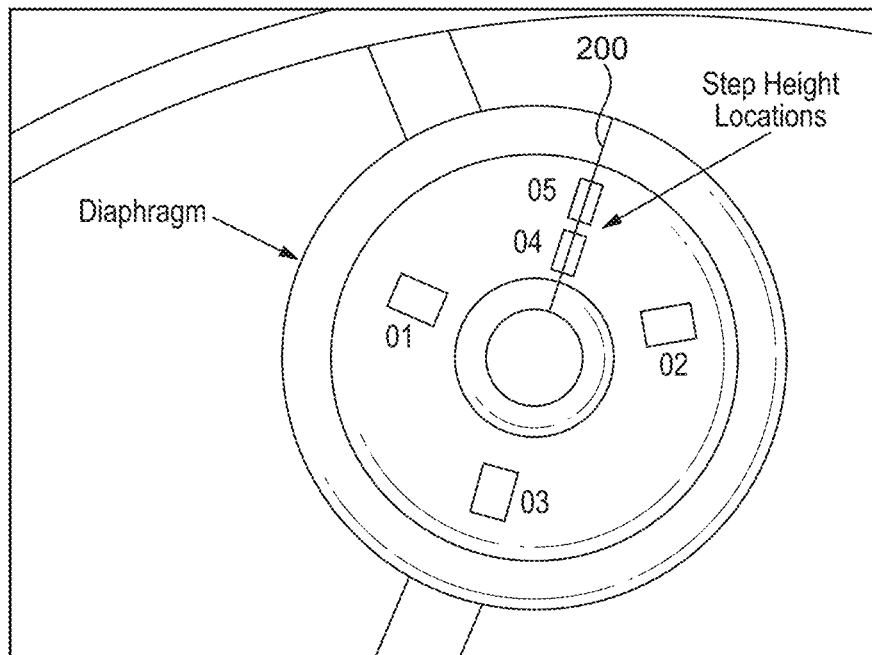


FIG. 13

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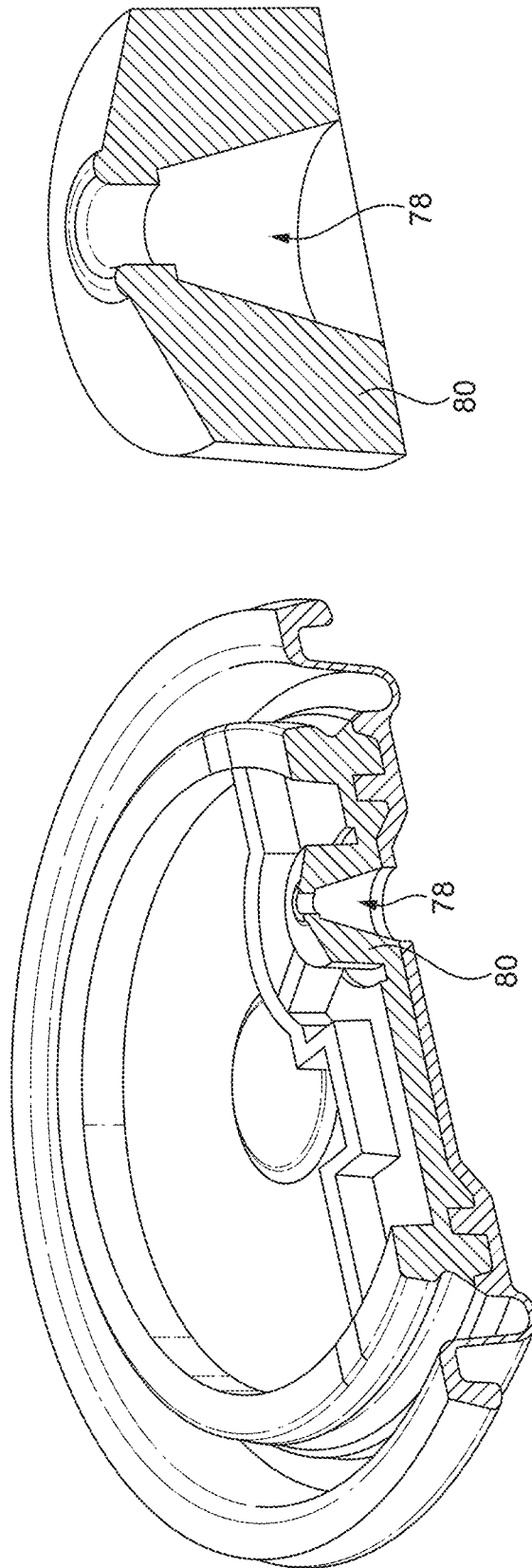


FIG. 14

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BREATH ACTUATED INHALER**CROSS-REFERENCE TO RELATED APPLICATION**

This application claims the benefit of priority of Great Britain Patent Application No. 1801309.4 filed on Jan. 26, 2018, the entire disclosure of which is incorporated herein by reference in its entirety for all purposes.

FIELD OF THE INVENTION

The present invention relates to a metered dose inhaler and, in particular, a breath actuated metered dose inhaler. The invention further provides valve port and a diaphragm for a pneumatic force holding unit of a breath actuated metered dose inhaler, a flap valve for the canister fire system of a breath actuated metered dose inhaler, as well as methods for manufacturing and assembling the same.

BACKGROUND TO IN THE INVENTION

Inhalers for delivering medicament to a patient by inhalation are known. Such devices include metered dose inhalers (of both pressurised and dry-powder types). Metered dose inhalers typically comprise a medicament-containing vessel and an actuator housing having a medicament delivery outlet in the form of a mouthpiece or nosepiece.

The medicament-containing vessel may be a pressurized canister containing a mixture of active medicament and propellant. Such canisters are usually formed from a deep-drawn aluminium cup having a crimped lid which carries a metering valve assembly. The metering valve assembly is provided with a protruding valve stem which, in use, is inserted as a tight push fit into a stem block in the actuator housing.

Metered-dose inhalers may either be of the manually operable type or the breath actuated type. For the manually operable type, the patient self-administers the medicament by manually pressing the closed end of the canister into the actuator housing to cause movement of the canister relative to its valve stem (which is fixed in the stem block of the actuator housing). This movement is sufficient to actuate the metering valve assembly of the canister, resulting in the pressurised contents of a metering chamber being vented through the stem, through the stem block and its exit orifice, and causing the medicament to exit the mouthpiece or nosepiece as an aerosol mist. Simultaneously with this action, the patient inhales through the nosepiece or mouthpiece, entraining the aerosol mist in the inhaled stream of air. The patient then releases the depression force on the canister which, under the action of an internal valve spring, moves upward with respect to the valve stem, returning to its resting position.

A more recent development is the so-called breath actuated metered-dose inhaler, which serves to automatically displace the canister relative to its valve stem and release the contents of the canister's metering chamber in response to a patient's inhalation. The general purpose of such inhalers is to alleviate difficulties in coordinating actuation of the metering valve assembly with the patient's inhalation, and to provide for a maximal amount of medication to be drawn into the patient's lungs.

A known breath actuated inhaler, disclosed in WO9209323A1 and WO0193933A2, which are incorporated herein by reference, has a pressurised canister and a metering valve for controlling the ejection of inhalable

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substances from the canister. The canister is operable by a force holding unit having a cap housing attachable to a main housing of the inhaler. In use, a mouthpiece cap is opened to prepare the inhaler ready for inhalation and then after inhalation the mouthpiece cap is closed to reset the force holding unit, i.e. return it to a rest configuration. The force holding unit holds the force for actuating the canister until it is required.

The force holding unit comprises a compression spring, a lower cap that engages the canister, a diaphragm attached to an upper surface of the lower cap, and a pivotally mounted flap valve for selectively sealing a valve port located in the diaphragm.

In use, when the mouthpiece cap is opened, the lower cap is forced downwards under the action of the compression spring. Then, as the lower cap moves down, an enclosed volume between the diaphragm and the lower cap is increased by a linear amount, and whilst valve port remains closed, this creates a pressure difference in the enclosed volume.

The offset of the differential between the pressure in the enclosed volume and atmospheric pressure results in the lower cap resisting action of the compression spring. Downward movement of the lower cap continues until the force is balanced between the force of the compression spring and the opposing forces of the pressure difference and metering valve. This is a prepared configuration.

The geometry of the mechanism is arranged such that the balance occurs before the valve has been actuated.

Flow of air across a vane on the flap valve during inhalation causes the valve to pivot, moving the flap valve seal out of its rest position, and opening a valve channel in the diaphragm. The subsequent passage of air into the volume between the diaphragm and the lower cap allows the volume to reach atmospheric pressure. The resulting imbalance of forces acting on the lower cap and canister produces the downward motion of the canister and actuation of the aerosol metering valve: releasing a measured dose through the dispensing nozzle and into the mouthpiece.

Referring to FIGS. 1 and 2 a known diaphragm assembly 640 for use with a breath actuated inhaler is shown.

The moulded flexible diaphragm 640 includes a rigid disc-like section 641, a flexible generally cylindrical wall section, or annular flexure 645, and a thicker connector section, or peripheral attachment ring 647. A central portion is unitarily formed with and extends radially inwardly from the annular flexure 645. The central portion is provided in the form of a disk bonded along a top surface to a bottom surface of the rigid disc-like section 641, i. e., surfaces substantially transverse to the central axis of the diaphragm 640.

The relatively thick disk-portion is moulded from a rigid material (relatively high stiffness) such as acrylonitrile butadiene styrene (ABS), which is particularly resistant to flexural deformation.

The relatively thin flexure portion which includes the central portion, the annular flexure 645 and the peripheral attachment ring 647, is moulded from an optimally flexible material (relatively low stiffness) such as a thermoplastic elastomer (TPE), permitting high performance. The multi-material diaphragm 640 may be manufactured using a multi-shot moulding process.

As shown in FIGS. 1 and 2, the central portion and the rigid disc-like section 641 both define a central upwardly extending boss 702 for additional strength. In addition, the rigid disc-like section 641 includes an outer axial wall 704 which provides further strength to the diaphragm 640. The

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central portion includes axial walls which are received within and bonded to axial grooves of the rigid disc-like section **641**, thereby providing bonding surfaces substantially parallel with the central axis of the diaphragm **640** and increasing the total bonding surface area between the central portion and the rigid disc-like section **641**.

In use, the peripheral attachment ring **647** of the diaphragm **640** is fitted around an annular wall of the lower cap and is secured in an air-tight manner thereon with a retainer ring by snap-fitting. The retainer ring also provides a snug fit for one end of the compression spring, such that the compression spring is thus located and free to act on the sleeve.

The valve channel **690** of the diaphragm **640** passes through the rigid disc-like section **641** and the central portion of the diaphragm. The valve channel **690** is closed by a valve seal (not shown), which is biased closed by a flat spring. The rigid disc-like section **641** of the diaphragm includes protrusions **712** extending upwardly therefrom that receive and correctly position a flat spring. The rigid disc-like section **641** of the diaphragm **640** also includes a baffle **714** on a top surface thereof for substantially preventing air flow between the valve seal and the diaphragm.

The rigid disc-like section **641** of the diaphragm **640** additionally includes an assembly location key **716** for use in correctly assembling the diaphragm **640** within the actuator assembly.

As better illustrated in FIG. **3**, a valve port **301** comprising an annular boss **302** defines the valve orifice channel **690**. The boss **302** comprises two radially outwardly extending projections **303**, **304** each defining a path through which polymer passed to form the boss **302** during injection moulding. The boss **302** comprises a circumferential side wall **307**, a radially extending upper surface **308**, including a sealing surface **309**. The radially outwardly extending projections **303**, **304** are circumferentially offset, and their upper surfaces **305**, **306** intersect the vertical side wall **307** of the boss **302**.

When using inhalers similar to those discussed above, it was observed that on occasion patients may not receive a measured dose upon inhalation, i.e. the canister does not fire.

Following these observations, an investigation by the inventors found that the missed dose of medicament may be because of unintentional actuation of the inhaler. The investigation found that the unintentional actuation may occur because of unintentional misuse leading to accidental actuation, said misuse including failing to use the inhaler immediately after priming.

More specifically, the inventors found that when in the prepared position the pressure difference maintained by the force holding degraded over a relatively short period of time, allowing the lower cap to progress in a canister fire direction under the action of the compression spring. This progression may continue until the canister fires.

Once the canister has fired accidentally as a result of the degradation of the pressure difference maintained by the force holding unit, the inhaler will not fire upon subsequent inhalation and the patient will not receive the intended dose of medicament.

The present invention aims to alleviate at least to a certain extent at least one of the problems of the prior art.

SUMMARY OF THE INVENTION

Accordingly, in a first aspect the invention provides an injection moulded polymer valve port for a pneumatic force holding unit in a breath actuated metered dose inhaler. The valve port comprises an annular boss defining a valve orifice

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channel. The valve port further comprises two, three, four or more, radially outwardly extending projections defining a path through which polymer passed to form the boss during moulding. The radially outwardly extending projections are substantially uniformly circumferentially separated. Typically extending from a circumferential outer wall of the annular boss. Preferably, their circumferential uniformity is offset by less than about 5 degrees, preferably by less than about 2 degrees. Typically, the boss has a longitudinal axis which passes through the valve orifice port, and two radially extending projections and the valve orifice port may lie in a common plane coincident with the longitudinal axis. In a preferred arrangement, the boss comprises two circumferentially uniformly separated radially outwardly extending projections, i.e. with a central angle of 180 degrees+/-5 degrees.

It has been found that by providing a boss with radially outwardly extending projections as described, the surface finish of the valve port, in particular, immediately adjacent the valve orifice is significantly improved, allowing a better seal to be formed with a valve port seal during use. The improved seal significantly reduces the rate of degradation of the pressure difference within a pneumatic force holding unit in a prepared configuration, reducing the likelihood of accidental actuation and the breath actuated inhaler not delivering medicament upon inhalation: improving patient compliance and treatment outcomes.

In a further aspect the invention provides an injection moulded polymer valve port for a pneumatic force holding unit in a breath actuated metered dose inhaler. The valve port comprises an annular boss defining a valve orifice channel. The valve port comprises one, two, or more radially outwardly extending projections defining a path through which polymer passed to form the boss during moulding, wherein an upper surface of the one or more radially outwardly extending projections and an upper surface of the annular boss are contiguous. Preferably, the upper surface of the annular boss and the upper surface of the projection are at an angle between about 90 degrees and about 180 degrees, preferably an obtuse angle, more preferably between 120 degrees and 180 degrees.

Advantageously, it has been found that because the upper surfaces are contiguous during moulding molten polymer flows along a mould path defining the projections and does no stall as it enters the chamber defining the boss. By way of comparison, during moulding of the boss illustrated in FIG. **3**, the molten polymer must travel vertically along an outer side surface of the boss from the upper surface of the projections to the boss' upper surface, stalling radial flow. Valve ports of the inventive arrangement have been found to have a surface finish that is significantly improved, in particular immediately adjacent the valve orifice. This facilitates a better sealing with a valve port seal during use. The improved seal significantly reduces the rate of degradation of the pressure difference within a pneumatic force holding unit in breath actuated inhaler in a prepared configuration, reducing the likelihood of accidental actuation and the breath actuated inhaler not delivering medicament upon inhalation: improving patient compliance and treatment outcomes.

In a further aspect the invention provides an injection moulded polymer valve port for a pneumatic force holding unit in a breath actuated metered dose inhaler, said valve port being located on a planar body and comprising an annular boss defining a valve orifice channel. The valve port further comprises one or more radially outwardly extending projections defining a path through which polymer passed to

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form the boss during moulding. A portion of the planar body immediately adjacent the boss has a depth that is less than or equal to a minimum thickness of the radially outwardly extending projection. Typically, the ratio of the depth of the portion immediately adjacent to the boss to the minimum thickness of the radially outwardly extending projection is from about 1:1 to about 1:2, preferably from about 1:1 to about 3:4. Typically, the portion of the planar body immediately adjacent the boss circumferentially encloses, preferably fully encloses, the boss between the one or more radially extending projections.

Typically, the portion of the planar body immediately adjacent the boss has a depth of from about 0.50 mm to about 0.70 mm, preferably from about 0.55 mm to about 0.65 mm. 0.60 mm is an example. The planar body is typically the relatively rigid disk-like portion of the diaphragm.

Additionally, or alternatively, the radially outwardly extending projections may have a thickness of from about 0.54 mm to about 0.83 mm, preferably from about 0.64 mm to about 0.73 mm. 0.68 mm is an example. Where there are two or more radially outwardly extending projections, typically they each have substantially the same thickness. The radially outwardly extending projections are typically drafted to aid mould release. In this instance the thickness relates to the minimum thickness of the projection.

Advantageously, it has been found that a boss that is surrounded by a narrowing (e.g. a narrowed portion of the planar body) concentrates polymer flow towards the upper surface of the boss during moulding. This has the effect of improving the surface finish of the valve port immediately adjacent the valve orifice, allowing a better seal to be formed with a valve port seal during use. The improved seal significantly reduces the rate of degradation of the pressure difference within a pneumatic force holding unit in a breath actuated inhaler in a prepared configuration, reducing the likelihood of accidental actuation and the breath actuated inhaler not delivering medicament upon inhalation: improving patient compliance and treatment outcomes.

In a further aspect the invention provides, a valve port for a pneumatic force holding unit in a breath actuated metered dose inhaler, said valve port comprising an annular boss with an inner wall defining a valve orifice channel wherein the volume of the orifice channel defined by the inner wall of the boss is greater than about 12.7° to of the volume of the boss, preferably from about 12.7% to about 20%, more preferably from about 13% to about 17%, 15.5% being an example, and/or wherein the inner wall defines a frustum of an imaginary cone with an apex angle of greater than about 20 degrees, preferably from about 22 degrees to about 35 degrees, more preferably from about 24 degrees to about 30 degrees. 28 degrees being an example.

Typically, the valve orifice channel has a cross-sectional area at its uppermost (i.e. sealing) end of from about 0.22 mm² to about 0.31 mm², 0.26 mm² being an example. Typically, the valve orifice channel has a substantially circular cross-section, typically along its entire length. Preferably, a portion of the wall of the valve orifice channel defines the frustum of an imaginary cone.

It has been found that by providing a boss with a high valve orifice channel volume to boss volume ratio, during injection moulding, polymer flow is concentrated towards the upper surface of the boss. Likewise, when the inner surface of the valve orifice defines the frustum of an imaginary cone with an apex of greater than 20 degrees. This has the effect of improving the surface finish of the valve port immediately adjacent the valve orifice channel opening,

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allowing a better seal to be formed with a valve port seal during use. As in other aspects, the improved seal significantly reduces the rate of degradation of the pressure difference within a pneumatic force holding unit of an inhaler in a prepared configuration, reducing the likelihood of accidental actuation and the breath actuated inhaler not delivering medicament upon inhalation: improving patient compliance and treatment outcomes.

In a further aspect the invention provides a valve port for a pneumatic force holding unit in a breath actuated metered dose inhaler, said valve port comprising a valve seal surface, which in use is engaged by a movable valve seal in a sealing arrangement, characterised in that the valve seal surface has a surface roughness average (RA) of 0.15 µm or less, preferably less than 0.12 µm, preferably from about 0.10 µm to about 0.01 µm.

Typically, the valve seal comprises an elastomer, preferably a thermoplastic elastomer. Preferably the thermoplastic elastomer is selected from the group consisting of styrenic block copolymers, thermoplastic olefins, thermoplastic polyurethanes, thermoplastic copolyester, thermoplastic polyimide. Advantageously thermoplastic elastomers can be injection moulded. Thermoplastic polyurethanes are particularly preferred.

The elastomer may have a hardness of from about 80 to 90 Shore A. Preferably this elastomer has a hardness of from about 82 to 87 Shore A (e.g. BASF Elastollan® 1185 A). Still more preferably, the elastomer has a hardness of about 85 Shore A.

In embodiments, the elastomer may comprise a blend of thermoplastic polyurethane elastomer and at least one release agent, typically in an amount of from about 2% to about 6% by weight, for example, Elastollan Konz. 950/1 4% from BASF.

Preferably the valve seal, when in a sealing arrangement, engages the valve seal surface with a moment of at least about 0.015 Nmm, preferably from about 0.017 Nmm to about 0.025 Nmm when in a rest configuration (e.g. with no vacuum), and from about 0.05 Nmm to about 0.11 Nmm when in a prepared configuration (e.g. with a vacuum).

The valve port may be manufacture using injection moulding; however, it will be appreciated that other methods may also be employed, e.g. spin casting, or an additive manufacturing technique: e.g. 3D printing.

By reducing the surface roughness of the valve port immediately adjacent the valve orifice an improved seal is formed with a valve port seal during use. As in other aspects, an improved seal significantly reduces the rate of degradation of the pressure difference within a pneumatic force holding unit in a prepared configuration, reducing the likelihood of accidental actuation and the breath actuated inhaler not delivering medicament upon inhalation: improving patient compliance and treatment outcomes.

In an aspect the invention provides a flap valve for the canister fire system of a breath actuated metered dose inhaler, wherein the flap valve comprises a chassis for pivotal mounting within the inhaler, a valve port according to any preceding claim, and a valve port seal mounted on the chassis configured to selectively engage the valve port in a sealing relation, and a vane for moving the valve port seal in direction away from the valve port in response to inhalation induced airflow.

In a further aspect the invention provides a diaphragm for a pneumatic force holding unit in a canister firing mechanism of a breath actuated metered dose inhaler comprising a valve port according to any previous aspect of the invention, or the flap valve according to the immediately preced-

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ing aspect. Typically, the diaphragm comprises a relatively rigid disk-like portion and relatively flexible membrane portion, and wherein the valve port is unitarily formed with the rigid disk-like portion.

The relatively rigid disk-like portion, including the valve port, is typically made from a rigid material (relatively high stiffness) such as acrylonitrile butadiene styrene, which is particularly resistant to flexural deformation. The relatively flexible portion which may include a central portion, an annular flexure and a peripheral attachment ring may be moulded from an optimally flexible material (relatively low stiffness) such as a thermoplastic elastomer. A thermoplastic polyurethane is particularly preferred.

The elastomer may have a hardness of from about 80 to 90 Shore A to about 35 to 40 Shore D. Preferably this elastomer has a hardness of from about 89 to about 90 Shore A and from about 37 to about 40 Shore D (e.g., BASF Elastollan® 1185 A). Still more preferably, the elastomer has a hardness of about 89 Shore A and about 37 Shore D.

Additionally, the elastomer comprises a blend of thermoplastic polyurethane elastomer and at least one release agent, typically in an amount of from about 2% to about 6% by weight, for example, Elastollan Konz. 950/1 4% from BASF.

In a further aspect the invention provides a mould for injection moulding a diaphragm for a breath actuated metered dose inhaler wherein the mould comprises cavities configured to produce a valve port, and/or diaphragm, according any earlier aspect of the invention. Preferably, the mould is metallic, typically steel, and has a surface average roughness (RA) of less than or equal to about 0.1 µm, preferably from about 0.025 µm to about 0.1 µm, preferably at least in the area corresponding to the sealing surface of the valve port. Typically, a SPI A3 finish is used the region of the sealing surface and a VDI-21 finish is used for the remainder of the diaphragm.

The invention further provides a method for manufacturing a diaphragm for a metered dose inhaler comprising the steps of providing a mould according to the immediately previous aspect and injecting molten polymer, or prepolymer, into the mould under pressure to form a diaphragm according to any preceding aspect of the invention.

Preferably the moulding is a two-shot moulding process. A first shot providing a relatively rigid disk like portion. A second shot providing a relatively flexible portion.

In the first shot; typically, molten polymer, e.g. ABS, is provided at a temperature of from about 220° C. to about 260° C., more preferably from about 240° C. to about 250° C., about 245° C. being an example. Typically, the polymer is injected, packed, and held at a pressure of from about 560 bar to about 840 bar, 700 bar being an example. Typically, the mould temperature is from about 30° C. to about 70° C., preferably from about 38° C. to about 48° C.: 43° C. being an example.

In the second shot, typically, molten polymer, e.g. TPE, is provided at a temperature of from about 205° C. to about 220° C., more preferably from about 205° C. to about 215° C., about 210° C. being an example. Typically, the polymer is injected, packed, and held at a pressure of from about 560 bar to about 840 bar, 700 bar being an example. Typically, the mould temperature is from about 15° C. to about 70° C.

For both the first shot and second shot, the hold time and pack time may be approximately 0.5 seconds each.

The injection time for the second shot is typically from about 0.10 seconds to about 0.15 seconds: 0.12 seconds being an example.

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The injection time for the first shot is preferably greater than about 0.5 seconds, more preferably from about 1 second to about 1.5 seconds: 1.26 second being an example. Whilst short injection times of from about 0.1 second to about 0.5 seconds may be employed, it has been found that a relatively long injection time for the first shot improves the surface finish of the diaphragm, in particular weld lines, on the upper surface of the boss, particularly at the sealing surface. During injection moulding of the valve port, the polymer passes through the mould cavity portions dimensioned to form the radially outwardly extending projection(s) into the mould cavity portion dimensioned to form the boss.

The invention further provides a breath actuated metered dose inhaler comprising a valve port, flap valve, and/or diaphragm according to or manufactured according to other aspects of the invention.

In a further aspect the invention provides a breath actuated metered dose inhaler comprising a canister fire system configured to fire a canister in response to patient inhalation, the canister fire system comprising a pneumatic force holding unit and having: a rest configuration in which a metering valve of the canister is in a refill configuration; a prepared configuration in which the canister fire system is actuatable by patient inhalation induced airflow; and a fire configuration in which the metering valve is in a dose delivery position. The pneumatic force holding unit is configured such that once the inhaler is moved from the rest configuration to the prepared configuration, in the absence of an external trigger, for instance patient inhalation induced airflow, the canister fire system remains in a prepared configuration for at least about 5 minutes, preferably at least about 15 minutes, more preferably at least about 30 minutes.

Typically, once the inhaler is moved from the rest configuration to the prepared configuration in 95% of instances the canister fire system will remain in a prepared configuration for at least about 15 minutes. Preferably; once the inhaler is moved from the rest configuration to the prepared configuration in 90% of instances the canister fire system will remain in a prepared configuration for at least about 30 minutes.

Advantageously, the significantly increased time to actuation reduces the likelihood of accidental actuation and the breath actuated inhaler not delivering medicament upon inhalation: improving patient compliance and treatment outcomes.

In a further aspect, the present invention provides a breath actuated metered dose inhaler comprising a canister fire system configured to fire a canister in response to patient inhalation, the canister fire system comprising a pneumatic force holding unit and having: a rest configuration in which a metering valve of the canister is in a refill configuration; a prepared configuration in which a canister actuation force is retained by the pneumatic force holding unit and the canister fire system is actuatable by patient inhalation induced airflow; and a fire configuration in which the metering valve is in a dose delivery position; wherein when in the prepared configuration the force retained by the pneumatic force holding unit degrades by less than about 6% over a period of 5 minutes, preferably less than about 3%, preferably from about 2.7% to about 0.08%: 1.5% being an example.

Advantageously, the significantly reduced rate of degradation of the pressure difference within a pneumatic force holding unit in a prepared configuration, reduces the likelihood of accidental actuation and, therefore, the breath

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actuated inhaler not delivering medicament upon inhalation; improving patient compliance and treatment outcomes.

It will be appreciated that all of the aspects and embodiments herein described may be combined mutatis mutandis. Specifically; each of the valve ports disclosed may have a sealing surface with a surface roughness average (RA) of less than of less than 0.15 μm , preferably less than about 0.1 μm .

BRIEF DESCRIPTION OF THE FIGURES

Preferred features of the present invention will now be described, by way of example; with reference to the accompanying drawings; in which:

FIG. 1-3 show a known multi-material diaphragm for a breath actuated inhaler;

FIG. 4 shows a multi-material diaphragm according to the invention;

FIG. 5-7 show cross-sections of a valve port according to the invention;

FIG. 8-9 shows a breath actuated metered dose inhaler according to the invention;

FIG. 10 shows an alternative diaphragm according to the invention;

FIG. 11 shows surface roughness testing results of a known valve port sealing surface;

FIG. 12 shows surface roughness testing results of a valve port sealing surface according to the invention,

FIG. 13 shows the locations at which surface roughness measurements may be taken.

FIG. 14 shows the volume of the boss and the valve orifice channel.

DETAILED DESCRIPTION OF THE INVENTION

The invention provides a valve port for a pneumatic force holding unit in a breath actuated metered dose inhaler, breath actuated metered dose inhalers; and methods of manufacturing and assembling the same.

FIG. 8 shows a breath actuated inhaler which is merely an example of an inhaler in accordance with the present invention. The inhaler includes a force holding unit housing 12, a main body 14, a mouthpiece dust cap 16 and a dose counter door 18 having a dose counter window. In other embodiments comprising nasal inhalers, the mouthpiece 66 may be replaced with a nose piece.

As shown by the exploded view of FIG. 8, a dose counter chamber 22 includes a dose counter system 24 closed within it by the dose counter door 18. The dose counter system includes an actuating pin 26 and return spring 28. The dose counter can take various forms and may, for example, be as described in EP2135199A or EP2514464A.

As also shown in FIG. 8, the inhaler 10 includes a force holding unit 30 which includes: a filter 32, flap valve housing 34, flap valve 36, flap valve spring 38, compression spring 40, retaining ring 42, diaphragm 44 and lower cap 46. The inhaler also includes a canister 50 with a metering valve 52 and a valve stem 54; as well as a yoke 56 with drive rods or legs 58 having distal ends 59 which are driven by respective cams 60 on the pivotally-connected mouthpiece dust cap 16. The valve stem 54 may be fitted into an inner bore of a valve stem block which communicates with a nozzle (not shown) for ejection of inhalable substances through a central bore of a mouthpiece 66 (FIG. 8) of the main body 14 of the inhaler.

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In embodiments, the arrangement of openings in the metering valve of the present invention is similar to those described in US2016/0084385, which is incorporated by reference herein. In particular, the metering valve of the present invention may be similar to the embodiment shown in FIG. 4 of US2016/0084385, in which the valve body includes at least one first opening (i.e., at least one first side hole 100 that is arranged in a cylindrical portion of the valve body) and at least one second opening (i.e., at least one second side hole 111 that, as with the first hole(s), is arranged in a cylindrical portion of the valve body), the second opening(s) being axially offset relative to the first opening(s) along a longitudinal axis that extends between a first axial end and a second axial end of the valve body. The first opening(s) and second opening(s) that are axially offset from each other along the valve body enable the metering chamber to be filled and emptied.

The force holding unit 30 operates substantially as disclosed with reference to FIGS. 1 to 3 of EP1289589A and the yoke 56 and mouthpiece dust cap 16 substantially as described in EP2514465A, including but not limited to FIG. 22 thereof, which are incorporated herein by reference.

FIG. 9 shows the flap valve 36 and diaphragm 44 in situ, in a patient inhalation configuration, so at the spring 38, the upper surface of the boss 80, and the valve orifice channel 78 are visible.

The canister 50 is operable by a force holding unit 30 having a cap housing 12 attachable to a main body 14 of the inhaler. In use, a mouthpiece cap 16 is opened to prime the inhaler ready for inhalation and then after inhalation the mouthpiece cap 16 is closed to reset the force holding unit 30, i.e. return it to a rest configuration.

In more detail, when the mouthpiece cap 16 is opened, the lower cap 46 is forced downwards under the action of the compression spring 40. Then, as the lower cap 46 moves down, an enclosed volume between the diaphragm 44 and the lower cap 46 is increased by a linear amount, and whilst valve port remains closed, this creates a pressure difference in the enclosed volume.

The offset of the differential between the pressure in the enclosed volume and atmospheric pressure results in the lower cap 46 resisting action of the compression spring 40. Downward movement of the lower cap 46 continues until the force is balanced between the force of the compression spring 46 and the opposing forces of the pressure difference and metering valve 52.

The geometry of the mechanism is arranged such that the balance occurs before the valve has been actuated.

Upon inhalation, air enters the inhaler through approximately ten air inlets 72 formed on the cap housing 12. Flow of air across a vane 74 on the flap valve 36 during inhalation causes the valve 36 to pivot, moving the flap valve seal 76 out of its rest position, and opening a valve orifice channel 78 in the diaphragm 44. The subsequent passage of air into the volume between the diaphragm 44 and the lower cap 46 allows the volume to reach atmospheric pressure. The resulting imbalance of forces acting on the lower cap 46 and canister 50 produces the downward (forward) motion of the canister 50 and actuation of the aerosol metering valve 52: releasing a measured dose through the dispensing nozzle and into the mouthpiece 66.

The force holding unit 30 relies on the described pressure difference to maintain the prepared configuration, and release thereof for firing the canister 50 under the action of the compression spring 40. The force holding unit 30 is therefore considered pneumatic within the normal meaning of the term.

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Referring to FIG. 4, a diaphragm 1000 according to the present invention for use with the medicament dispenser of FIGS. 8 and 9 is shown.

The moulded flexible diaphragm 1000 includes a rigid disc-like section 1041, a flexible generally cylindrical wall section, or annular flexure 1045, and a thicker connector section, or peripheral attachment ring 1047. A central portion (not shown) is unitarily formed with and extends radially inwardly from the annular flexure 1045. The central portion preferably is provided in the form of a disk bonded along a top surface to a bottom surface of the rigid disc-like section 1041.

The relatively thick disk-portion which includes the disc-like section 1041 of the diaphragm 1000, is moulded from acrylonitrile butadiene styrene, which is particularly resistant to flexural deformation. The relatively thin flexure portion which includes the central portion, the annular flexure 1045 and the peripheral attachment ring 1047, is moulded from thermoplastic polyurethane, permitting high performance flexibility. The multi-material diaphragm 1000 may be made using a multi-shot moulding process wherein the rigid disc-like section is moulded in a first step, and the second flexible portion is moulded in a second step, and at the same time bonded to the first portion.

As shown in FIG. 4, the rigid disc-like section 1041 defines a central upwardly extending boss 1002 for additional strength. In addition, the rigid disc-like section 1041 includes an outer axial wall 1004 which provides further strength to the diaphragm 1000.

The valve port 1095 of the diaphragm 1000 passes through the rigid disc-like section 1041 and the central portion of the diaphragm. The valve port 1095 is closed by the valve port seal 76, which is biased closed by a flat spring 38, as shown in FIG. 9. Although not shown, the rigid disc-like section 1041 of the diaphragm may include protrusions extending upwardly therefrom that receive the flat spring 38. The rigid disc-like section 1041 of the diaphragm 1000 also includes a baffle 1014 on a top surface thereof for substantially preventing air flow between the valve port seal 76 and the diaphragm.

As illustrated in FIG. 4 the valve port 1095 comprises an annular boss 1100 projecting from an upper surface of the rigid disc-like portion 1041 of the diaphragm. Typically, the annular boss 1100 and rigid disc-like portion 1041 are a single unitary structure. The annular boss 1100 comprises a lower generally cylindrical body portion 1101 and an upper portion 1102 in the form of a truncated cone. The frustum of the truncated cone provides the upper surface 1103 of the annular boss 1100. The upper surface 1103 includes an annular projection 1104 which surrounds the entrance to the valve orifice channel and provides the sealing surface 1103, which in use engages the valve port seal in a sealing relation. Whilst the illustrated annular boss 1100, including both its upper 1102 and lower portions 1101, and the annular projection 1104, all have a circular circumference, it will be appreciated that other boss shapes may also be employed without departing from the invention. Accordingly, unless stated otherwise, for the purposes of the invention the use of annular, circumference, circumferential and/or radial, or the like, do not restrict the invention to circular cross-sectioned bodies. Equally, substantially circular cross-sectioned and/or circumferenced bodies are not excluded.

As illustrated, the valve port 1095 further comprises two radially outwardly extending projections 1106 and 1107. A first projection 1106 extending from outer wall 1004 to the annular boss 1100. The second projection extending from the baffle 1014 to the annular boss 1100. During moulding

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molten polymer, or prepolymer, flows along a path defined by the mould corresponding to each of the two projections 1106 1107 into the annular boss mould cavity. Typically, the projections are of substantially the same thickness 'T'. In this illustrated embodiment 0.64 mm. The illustrated projections 1106 1107 are substantially uniformly circumferentially separated. That is to say, each and every projection is separated from its adjacent projections by substantially the same central angle. The illustrated projections 1106 1107 are separated from each other by a central angle of 180 degrees. They are diametrically opposed. As illustrated by reference to FIG. 5 and FIG. 6, an imaginary straight-line Y running along a central axis of the projections passes through the central longitudinal axis X of the valve orifice channel. This arrangement concentrates polymer flow towards the centre of the boss 1100 during moulding, improving the surface finish of the upper surface 1103 and in particular its sealing surface 1105.

As better illustrated in FIG. 6, the upper surfaces of the first 1107 and the second projections 1106 are both contiguous with the upper surface 1103 of the annular boss 1100. The upper surface 1110 of the first projection 1107 and the upper surface 1103 of the annular boss 1100 are at an angle (α) of greater than 90 degrees but less than 180 degrees. The upper surface 1109 of the second projection 1106 and the upper surface 1103 of the annular boss 1100 are at an angle (β) of approximately 180 degrees: preferably there is no discernible joint between the two.

As a result of each of the upper surfaces 1109 1110 of the projections 1106 1107 and the upper surface 1103 of the annular boss 1100 joining directly, during moulding, molten polymer is able to flow directly along the mould surface from projection upper surface to boss upper surface without stalling, improving the finish of the upper surface 1103 of the annular boss 1100 and in particular the sealing surface 1105.

As illustrated in FIG. 6 a portion of the valve orifice channel forms the frustum of an imaginary cone with an apex angle θ of 28 degrees. With reference to FIG. 14, the valve orifice channel 78 has a volume of 1.91 mm³ and the annular boss 80 has a volume of 12.02 mm³.

As better illustrated in FIGS. 5 and 7, the annular boss 1100 is surrounded by a circumferential channel 1111 formed in the upper surface of the diaphragm 1041 surrounding the annular boss 1100. The channel 1111 has two sections 1112 and 1113 each extending between the two projections 1106 and 1107 around opposite sides of the annular boss 1100. The channel sections 1112 and 1113 reduce the depth of the relatively rigid disc-like portion 1041 of the diaphragm immediately adjacent to the annular boss; typically, to a depth 'D' less than the thickness 'T' of the projections 1106 and 1107. This arrangement concentrates polymer flow towards the centre of the annular boss 1100 during moulding, improving the smoothness of the upper surface 1103 and in particular the sealing surface 1105.

FIG. 10 shows an alternative diaphragm central disk 1041 according to the invention. As illustrated, this embodiment differs from that illustrated in FIG. 4 in that one of the radially outwardly extending projections 1210 of the valve port 1095 extends from the annular boss 1100 to the central upwardly extending boss 1002. As with the valve port 1095 shown in FIG. 4, this arrangement concentrates polymer flow towards the centre of the annular boss 1100 during moulding, improving the smoothness of the upper surface 1003 and, in particular, the sealing surface 1005.

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Advantageously, it has been found that injection moulded diaphragms according to the invention provide an increased yield during manufacturing compared to those illustrated in FIGS. 1-3 and improved surface finish immediately adjacent the valve channel orifice. In embodiments, the yield has increased from about 50% to about 85%.

In embodiments the breath actuated metered dose inhaler comprises a reservoir, particularly a pressurized canister, comprising an active pharmaceutical ingredient (API).

Preferably the active pharmaceutical ingredient is presented in a pharmaceutical composition comprising a propellant, optionally a co-solvent and optionally other pharmaceutically acceptable excipients.

Preferred propellants include hydrofluoroalkanes, in particular 1,1,1,2-tetrafluoroethane (HFA134a), 1,1,1,2,3,3,3-heptafluoropropane (HFA227), or combinations thereof. Most particular propellant is HFA134a. Most particular HFA134a concentration is from about 91.8% w/w to 92.9% w/w.

HFA134a has a low boiling point (-261°C.) and correspondingly high vapor pressure (572 kpa) at 20°C.

Particular co-solvents are selected from the list of aliphatic alcohols (particularly ethanol), glycerols and glycols. Most particular co-solvent is ethanol. Most particular ethanol concentration is about 8% w/w.

Ethanol is well known to be compatible with HFA-134a and increases the solubility of BDP. Ethanol (anhydrous) is used as a co-solvent to aid solubility of BDP in HFA134a. A concentration of around 8% w/w of ethanol is known to provide necessary stability, preventing precipitation and achieving correct aerosol performance.

Other pharmaceutically acceptable excipients include surfactants, particularly oleic acid.

Preferably, the active pharmaceutical ingredient is suspended in the propellant. Alternatively, the active pharmaceutical ingredient is dissolved in the propellant. The active pharmaceutical ingredient may also be partly suspended and partly dissolved in the propellant.

A particular active pharmaceutical ingredient is selected from the group consisting of anti-inflammatory agents, β 2-adrenoreceptor agonists, anti-cholinergic agents, antihistamines, serotonin agonists, and combinations thereof.

Suitable anti-inflammatory agents include corticosteroids and NSAIDs.

Suitable corticosteroids which may be used include those oral and inhaled corticosteroids and their pro-drugs which have anti-inflammatory activity. Examples of suitable corticosteroids include methyl prednisolone, dexamethasone, fluticasone propionate, fluticasone furoate, beclomethasone, beclomethasone esters such as e.g. the 17-propionate ester or the 17,21-dipropionate ester, budesonide, flunisolide, mometasone, mometasone esters such as e.g. the furoate ester, triamcinolone acetonide, rofleponide, ciclesonide, and butixocort propionate.

A particular corticosteroid is beclomethasone dipropionate (BDP).

Suitable NSAIDs include sodium cromoglycate, nedocromil sodium, phosphodiesterase (PDE) inhibitors (e. g. theophylline, PDE4 inhibitors or mixed PDE3/PDE4 inhibitors), leukotriene antagonists, inhibitors of leukotriene synthesis, iNOS inhibitors, tryptase and elastase inhibitors, beta-2-integrin antagonists and adenosine receptor agonists or antagonists (e. g. adenosine 2a agonists), cytokine antagonists (e.g. chemokine antagonists) or inhibitors of cytokine synthesis.

Suitable β 2-adrenoreceptor agonists are selected from SABA (short-acting β 2-adrenoreceptor agonists), LABA

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(long-acting β 2-adrenoreceptor agonists), ultra-LABA (ultra-long-acting β 2-adrenoreceptor agonists), and combinations thereof.

Suitable SABA include bitolterol, fenoterol, isoprenaline, orciprenaline, pirbuterol, procaterol, salbutamol, levosalbutamol, terbutaline, and pharmaceutically acceptable salts and esters thereof.

Suitable LABA include bambuterol, clenbuterol, formoterol, arformoterol, protokylol, salmeterol, and pharmaceutically acceptable salts and esters thereof.

Suitable ultra-LABA include indacaterol, olodaterol, vilanterol, and pharmaceutically acceptable salts and esters thereof.

Particularly suitable β 2-adrenoreceptor agonists include salmeterol xinafoate, salbutamol sulphate, salbutamol free base, formoterol fumarate, fenoterol or terbutaline.

A particular β 2-adrenoreceptor agonist is salbutamol sulphate.

Suitable anticholinergic agents are those compounds that act as antagonists at the muscarinic receptor, in particular those compounds, which are antagonists of the M1 and M2 receptors. Compounds include the alkaloid of the belladonna plants as illustrated by the likes of atropine, scopolamine, homatropine, hyoscyamine; these compounds are normally administered as a salt, being tertiary amines.

Particularly suitable anticholinergics include ipratropium (e.g. as the bromide), oxitropium (e. g. as the bromide) and tiotropium (e. g. as the bromide). Further suitable anticholinergics of interest are methantheline, propantheline bromide, anisotropine methyl bromide, clidinium bromide, copyrolate, isopropamide iodide, mepenzolate bromide, tridihexethyl chloride, hexocyclium, cyclopentolate hydrochloride, tropicamide, trihexyphenidyl hydrochloride, pirenzepine, telenzepine, and methoctramine.

Suitable antihistamines (also referred to as H1-receptor antagonists) include carbinoxamine maleate, clemastine fumarate, diphenylhydramine hydrochloride, dimenhhydrinate, pyrilamine maleate, tripeleminamine HCl, tripeleminamine citrate, chlorpheniramine, chlorpheniramine maleate, acrivastine, hydroxyzine HCl, hydroxyzine pamoate, cyclizine HCl, cyclizine lactate, meclizine HCl, cetirizine HCl, astemizole, levocabastine HCl, loratadine, loratadine descarboethoxy analogue, terfenadine, fexofenadine hydrochloride, azelastine hydrochloride.

In a particular embodiment of the invention, the active pharmaceutical ingredient is selected from beclomethasone dipropionate (BDP), salbutamol sulphate and dihydroergotamine.

In a particular embodiment the breath actuated metered dose inhaler comprises a pressurized canister comprising beclomethasone dipropionate as active pharmaceutical ingredient; HFA134a as propellant and ethanol as co-solvent.

In a particular embodiment the breath actuated metered dose inhaler comprises a pressurized canister comprising beclomethasone dipropionate as active pharmaceutical ingredient at about 1.0 mg/ml, HFA134a as propellant at about 1090.20 mg/ml and ethanol as co-solvent at about 94.80 mg/ml.

In a particular embodiment the breath actuated metered dose inhaler comprises a pressurized canister comprising beclomethasone dipropionate as active pharmaceutical ingredient at about 0.084% w/w, HFA134a as propellant at about 91.9% w/w and ethanol as co-solvent at about 8.0% w/w.

In a particular embodiment the breath actuated metered dose inhaler comprises a pressurized canister comprising

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beclo-methasone dipropionate as active pharmaceutical ingredient at about 0.169% w/w, HFA134a as propellant at about 91.8% w/w and ethanol as co-solvent at about 8.0% w/w.

In a particular embodiment the breath actuated metered dose inhaler comprises a pressurized canister comprising salbutamol sulphate as active pharmaceutical ingredient, HFA134a as propellant and ethanol as co-solvent.

In a particular embodiment the breath actuated metered dose inhaler comprises a pressurized canister comprising about 0.1098 mg of salbutamol sulphate as active pharmaceutical ingredient, about 27.8 mg of HFA134a as propellant and about 3.6 mg of ethanol as co-solvent.

One embodiment relates to a breath actuated metered dose inhaler as described herein comprising an active pharmaceutical ingredient.

One embodiment relates to a breath actuated metered dose inhaler as described herein comprising an active pharmaceutical ingredient for therapeutic use.

One embodiment relates to a breath actuated metered dose inhaler as described herein comprising an active pharmaceutical ingredient for use in the treatment or prevention of a respiratory disease, particularly COPD or Asthma.

One embodiment relates to an active pharmaceutical ingredient for use in the treatment or prevention of a respiratory disease, particularly COPD or Asthma, wherein the active pharmaceutical ingredient is delivered to a patient using a breath actuated metered dose inhaler as described herein.

One embodiment relates to a method for the treatment or prevention of respiratory diseases, particularly COPD or Asthma, which method comprises administering an active pharmaceutical ingredient to a human being or animal using a breath actuated metered dose inhaler as described herein.

One embodiment relates to the use of a breath actuated metered dose inhaler as described herein comprising an active pharmaceutical ingredient for the treatment or prevention of respiratory diseases, particularly COPD or Asthma.

The invention will now be illustrated by the way of the following examples which are intended to be non-limiting.

Examples

Sample Preparation

Two groups of Easi-Breathe™ inhaler force holding unit diaphragms were prepared for use in the following examples.

The diaphragms in both groups shared the following common features.

The diaphragms of both groups were injection moulded on a Nestal 120 2-shot apparatus with 8+8 cavity mould and 25 mm/25 mm screw and barrel. In both groups the rigid disk-like portion was made from ABS Sabic Cyclocac™ HMG47MD, and the central portion, the annular flexure and the peripheral attachment ring were moulded from an elastomer comprising 96% BASF Elastollan® 1185A with 4% BASF Konz 950/1 additive as release agent.

The first “control” group diaphragms (M30579) were manufactured according to FIGS. 1 to 3, with the injection moulding parameters as set out in Table 1.

Whereas, the second “test” group diaphragms (M24406) were manufactured according to FIG. 4, with the injection moulding parameters as set out in Table 2.

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TABLE 1

Parameter	Process Value	Minimum Value	Maximum Value
Diaphragm-M24406			
Injection Time	.13 sec.	.12 sec.	.14 sec.
Hold Pressure	750 bar	675 bar	825 bar
Pack and Hold Time	1.0 sec	.9 sec	1.1 sec
Cool Time	6.0 sec	5.4 sec	6.6 sec
Barrel Temp.	210° C.	205° C.	215° C.
Mold Water (Front/Cavities)	75° F.	65° F.	85° F.
Mold Water (Back/Cores)	75° F.	65° F.	85° F.
2nd Shot			
Injection Speed	10 mm/s	9 mm/s	11 mm/s
Pack and Hold Pressure	700 bar	630 bar	770 bar
Total Pack and Hold Time	1.0 sec.	1.0 sec.	1.0 sec
Cool Time	6.0 sec.	6.0 sec.	6.0 sec.
Barrel Temp.	245° C.	240° C.	250° C.

TABLE 2

Parameter	Process Value	Minimum Value	Maximum Value
Diaphragm-M30579			
Injection Time	1.26 sec.	1.13 sec.	1.39 sec.
Hold Pressure	10153 psi	8122 psi	12183 psi
Pack and Hold Time	700 bar	560 bar	840 bar
Cool Time	1.0 sec	1.0 sec	1.0 sec
Melt Temp.	6.0 sec	6.0 sec	6.0 sec
Mold Temp.	473° F.	463° F.	483° F.
Mold Water (Front/Cavities)	245° C.	240° C.	250° C.
Mold Water (Back/Cores)	110° F.	100° F.	120° F.
Mold Water (Back/Cores)	43° C.	38° C.	48° C.
2nd Shot			
Injection Time	0.12 sec.	0.108 sec.	0.132 sec.
Pack and Hold Pressure	10153 psi	8122 psi	12183 psi
Total Pack and Hold Time	700 bar	560 bar	840 bar
Cool Time	1.0 sec.	1.0 sec.	1.0 sec
Melt Temp.	6.0 sec.	6.0 sec.	6.0 sec.
Mold Temp.	410° F.	400° F.	420° F.
	210° C.	205° C.	215° C.

Surface Roughness

The surface roughness of the sealing surface of each diaphragm was analysed using Bruker Contour GT white light interferometry machine at a magnification of 27.5x. Three areas of were scanned on each sealing surface, i.e. those indicated by the three-pronged arrow in FIG. 13. Each scanning area was 230 μm x 172 μm. The areas were selected so as to avoid any weld line.

The results are summarised in Table 3. The results show that the test diaphragms are less rough than control diaphragms.

Weld Line Measurements

Using the Bruker Contour GT, the step height measurement mode was used to measure the depth of the weld line of the diaphragm samples and the step width measurement mode and Cross Sectioning was used to measure the width of the weld line. The location of the measurements are indicated in FIG. 13 by rectangles 4 and 5: labelled ‘Step

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Height Locations". The weld line (200) is indicated. Example results are illustrated in FIGS. 11 and 12, and summarised in Table 3.

TABLE 3

	Control Diaphragm Design (n = 2)	Test Diaphragm Design (n = 2)
Mean Roughness	0.162	0.095
Average (RA)/ μm		
Mean Weld Line Depth/ μm	11	13.95

Force Holding Unit Performance

Otherwise identical EasiBreathe™ force holding units (FHUs) were assembled comprising either the control or test diaphragms mentioned above. The ability of both types of FHU to retain a pressure difference after priming was then assessed using an Instron 5564 force testing unit according to the following method. The Instron was equipped with an Instron ± 1 kN load cell and operated using Bluehill 2.33.895 software.

The FHU to be tested was secured in the Instron, with the Instron gripping the unit housing and the lower cap. The Instron was then used to compress the FHU until a force of 90N was achieved. Then the Instron was backed off 2.6 mm and a first, F1, force reading was recorded. The Instron was held in the same position for a period of 5 minutes, after which time a second force reading, F2, was taken.

The results are summarised in Tables 4 and 5.

TABLE 4

	Control Diaphragm Design (n = 10)		
	F1 (N)	F2 (N)	Delta F1 - F2 (N)
Mean	23.14	27.39	4.25
Minimum	22.72	24.34	1.48
Maximum	23.63	34.35	11.52

TABLE 5

	Test Diaphragm Design (n = 10)		
	F1 (N)	F2 (N)	Delta F1 - F2 (N)
Mean	21.701	22.034	0.333
Minimum	20.74	21.33	0.18
Maximum	22.2	22.42	0.59

As demonstrated, FHUs containing the test diaphragms according to the invention were able to maintain a pressure difference more effectively over the allotted time period.

The invention claimed is:

1. A breath actuated metered dose inhaler comprising:

a canister fire system configured to provide a canister actuation force to fire a medicament containing canister in response to patient inhalation, the canister fire system comprising a pneumatic force holding unit and having:

a rest configuration in which a metering valve of the canister is in a refill configuration;

a prepared configuration in which a canister actuation force is retained by a difference in pressure between an enclosed volume within the pneumatic force holding unit and atmospheric pressure, and in which prepared

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configuration the canister fire system is actuatable by patient inhalation induced airflow;
and a fire configuration in which the metering valve is in a dose delivery position;

wherein, in the prepared configuration, the force retained by the pneumatic force holding unit reduces but by less than about 6% over a period of 5 minutes.

2. The breath actuated metered dose inhaler of claim 1, wherein, when in the prepared configuration, the force retained by the pneumatic force holding unit reduces by less than about 3% over a period of 5 minutes.

3. The breath actuated metered dose inhaler of claim 1, further comprising at least one of:

a valve port for the pneumatic force holding unit, the valve port comprising an annular boss defining a valve orifice channel and two or more radially outwardly extending projections defining a path through which polymer passes to form the annular boss during injection molding, wherein the two or more radially outwardly extending projections are substantially uniformly circumferentially separated and the annular boss has a longitudinal axis which passes through the valve orifice channel, and wherein the at least two radially outwardly extending projections and the valve orifice channel lie in a common plane coincident with the longitudinal axis;

a flap valve comprising a chassis for pivotal mounting within the inhaler, a valve port seal mounted on the chassis configured to selectively engage the valve port in a sealing relation, and a vane for moving the valve port seal away from the valve port in response to inhalation induced airflow; and

a diaphragm comprising a rigid disk portion and a flexible membrane,

wherein the valve port is unitarily formed with the rigid disk portion.

4. The breath actuated metered dose inhaler according to claim 1 comprising a medicament for use in the treatment of a respiratory disease.

5. The breath actuated inhaler according to claim 4 wherein the respiratory disease is selected from COPD and asthma.

6. The breath actuated inhaler according to claim 5 wherein the medicament is selected from the group consisting of an anticholinergic and a corticosteroid.

7. The breath actuated inhaler according to claim 6, wherein the anticholinergic comprises tiotropium.

8. The breath actuated inhaler according to claim 6, wherein the corticosteroid comprises beclomethasone dipropionate.

9. The breath actuated inhaler of claim 1 wherein the pneumatic force holding unit comprises a valve port comprising a valve seal surface configured to be sealably engaged by a movable valve seal, wherein the valve seal surface has a surface roughness average (RA) of less than about 0.15 μm .

10. A breath actuated metered dose inhaler comprising: a canister fire system configured to provide a canister actuation force to fire a medicament containing canister in response to patient inhalation, the canister fire system comprising a pneumatic force holding unit and having:

a rest configuration in which a metering valve of the canister is in a refill configuration;

a prepared configuration in which a canister actuation force is retained by a difference in pressure between an enclosed volume within the pneumatic force holding

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unit and atmospheric pressure, and in which prepared
configuration the canister fire system is actuatable by
patient inhalation induced airflow;
and a fire configuration in which the metering valve is in
a dose delivery position;
wherein, in the prepared configuration, the force retained
by the pneumatic force holding unit reduces but by less
than about 6% over a period of 5 minutes and wherein
the pneumatic force holding unit further comprises a
valve port comprising a relatively rigid valve seal
surface configured to be sealably engaged by an elas-
tomer valve seal, wherein the relatively rigid valve
seal surface has a surface roughness average (RA) of
less than about 0.15 μm .

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EXHIBIT I

(12) **United States Patent**
Buck et al.

(10) **Patent No.:** **US 11,395,888 B2**
(45) **Date of Patent:** **Jul. 26, 2022**

(54) **INHALERS AND RELATED METHODS**

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(71) Applicant: **Norton (Waterford) Limited,**
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(72) Inventors: **Daniel Buck,** County Waterford (IE);
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(*) Notice: Subject to any disclaimer, the term of this
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Primary Examiner — Elliot S Ruddie

(74) *Attorney, Agent, or Firm* — Morgan, Lewis &
Bockius LLP

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(30) **Foreign Application Priority Data**

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A61M 15/00 (2006.01)

A61M 15/08 (2006.01)

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(52) **U.S. Cl.**

CPC **A61M 15/0066** (2014.02); **A61K 9/0073**
(2013.01); **A61K 31/46** (2013.01);

(Continued)

(58) **Field of Classification Search**

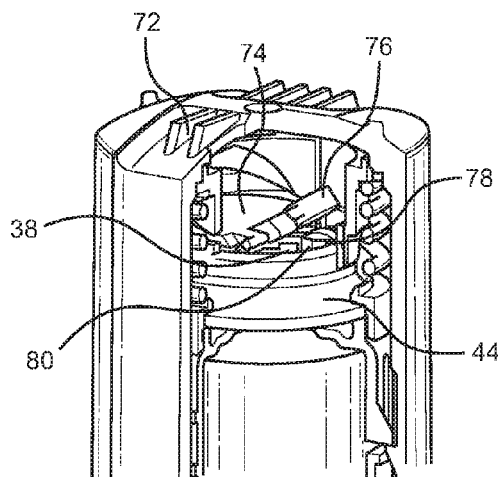
CPC A61M 15/0066; A61M 15/0013; A61M
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(57) **ABSTRACT**

An inhaler housing (14) for an inhaler (10) for inhaling inhalable substances, the inhaler having: a body (14) and a dose counter (24) with a return spring (28), wherein a distinct guide surface (162) is provided for guiding the end of the return spring into a recess (152), the distinct guide surface being wider than an entrance mouth (160) of the recess, a dose counter chamber (22) being provided which is separated from a tubular interior space (182) of the inhaler by a barrier (180), the barrier including a stepped upper wall area (184) including at least three steps (186, 188, 190, 192) at different levels, the inhaler having a valve stem block (62) having an inner bore and a valve stem block having a seal (224) in the inner bore with a second diameter which is smaller than a first diameter of the inner bore, the inhaler having a canister (150) being adapted to move during operation between 1 and 4 mm, a drive being arranged to apply a firing force of between 15 N and 60 N of force to the canister at a position of the canister relative to a valve stem (54) at which the canister fires.

30 Claims, 21 Drawing Sheets



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(2013.01); *A61M 15/0013* (2014.02); *A61M*
15/0021 (2014.02); *A61M 15/0025* (2014.02);
A61M 15/0071 (2014.02); *A61M 15/0091*
(2013.01); *A61M 15/08* (2013.01); *A61P*
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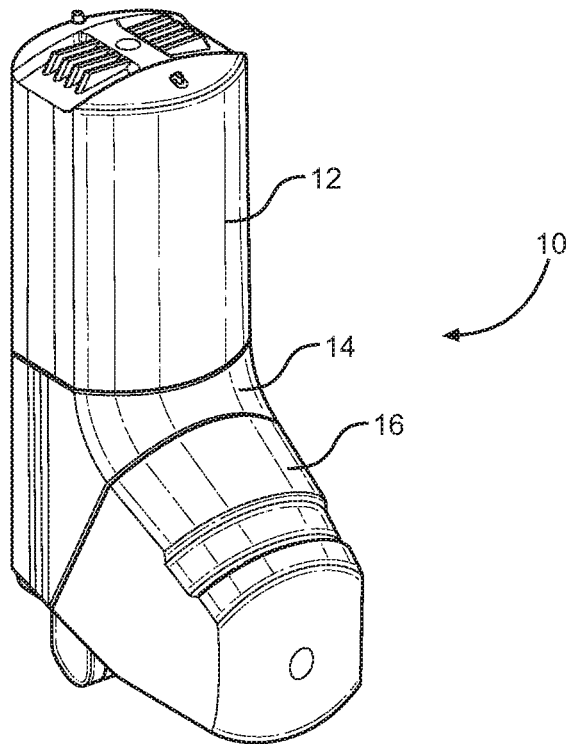


FIG. 1A

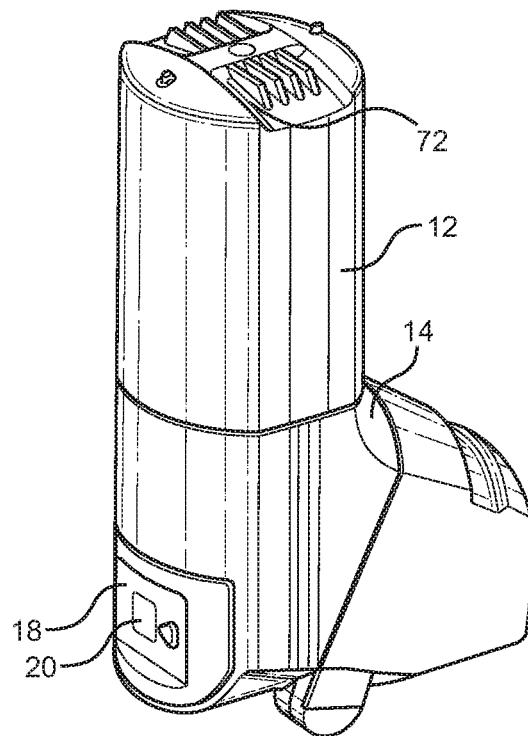
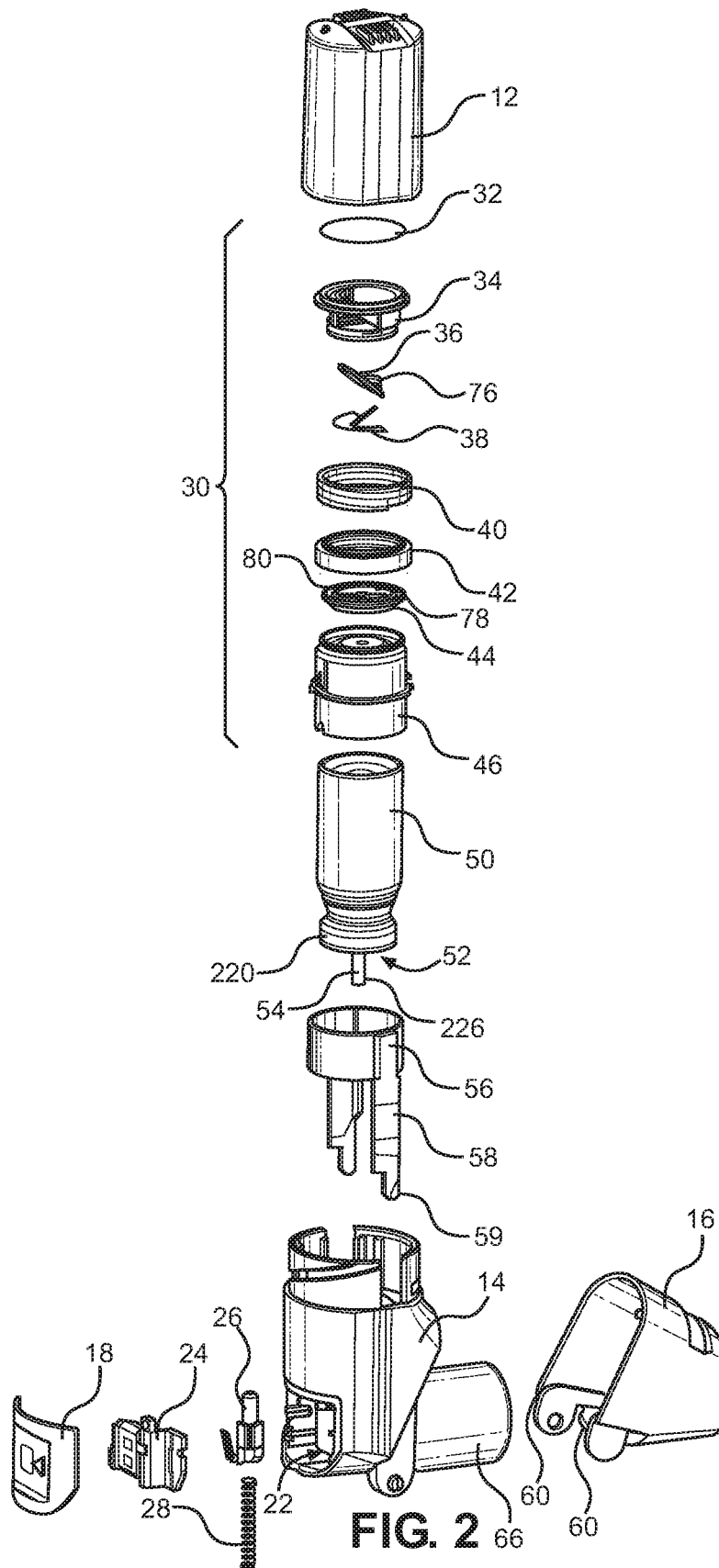


FIG. 1B



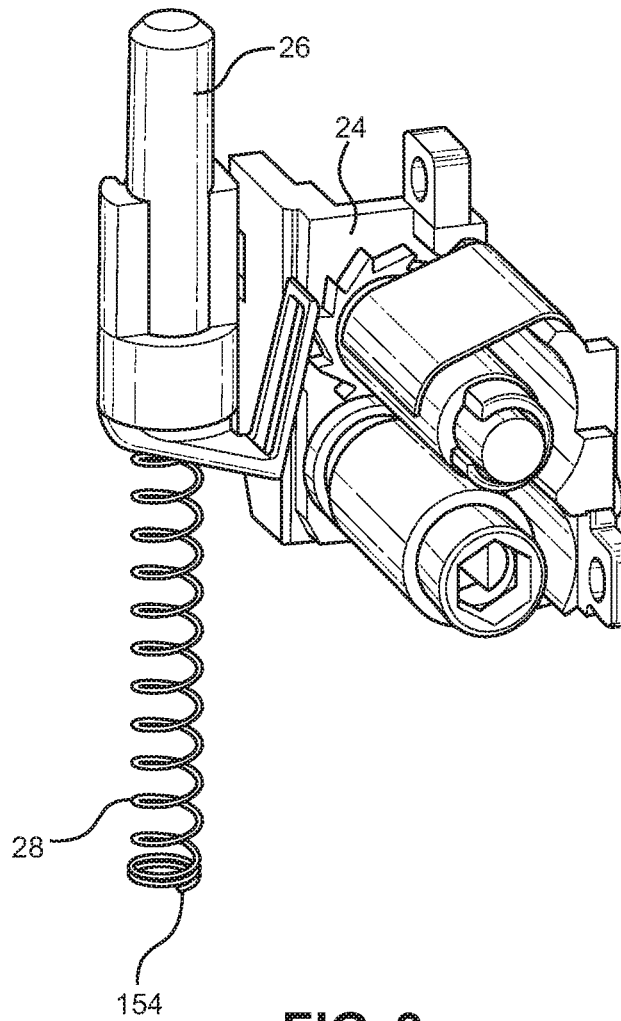


FIG. 3

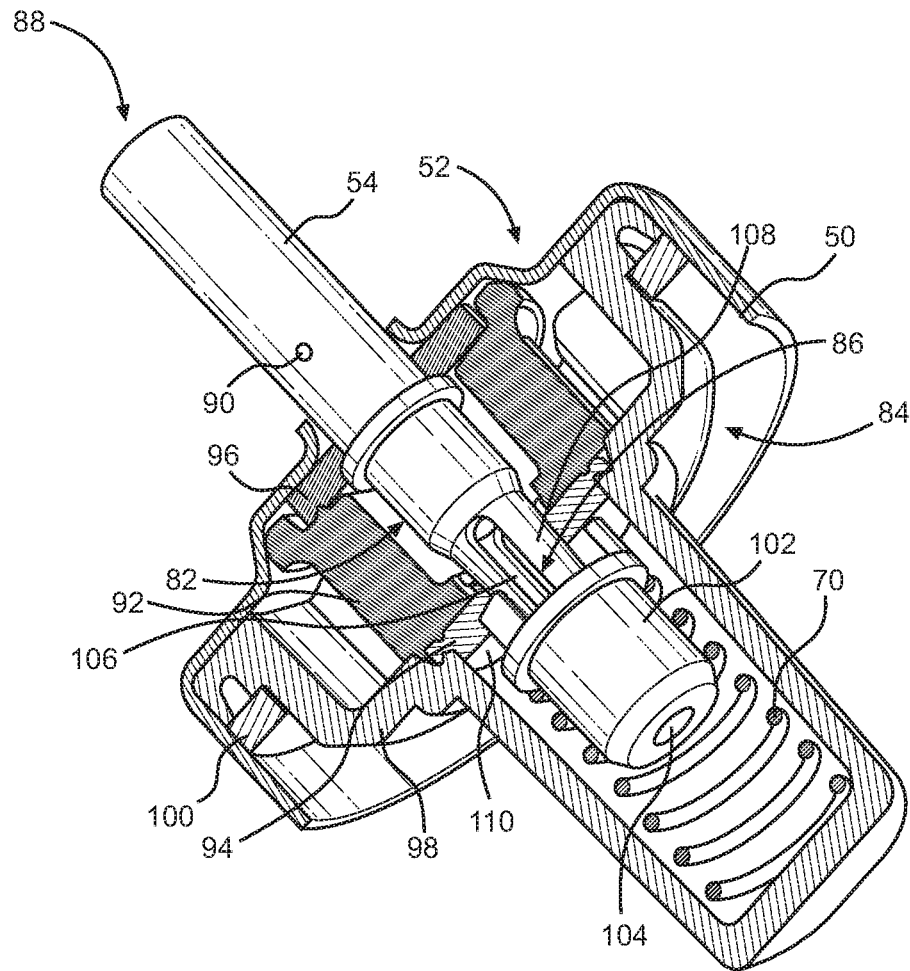


FIG. 4

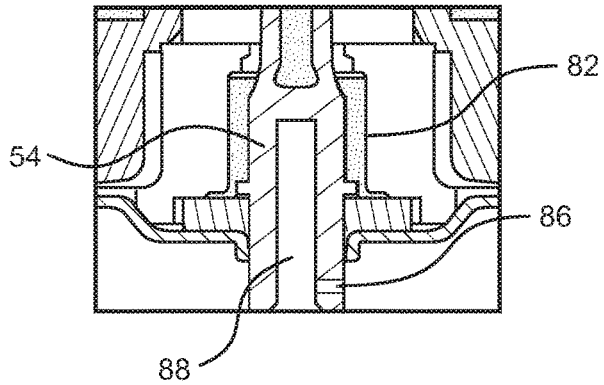


FIG. 5A

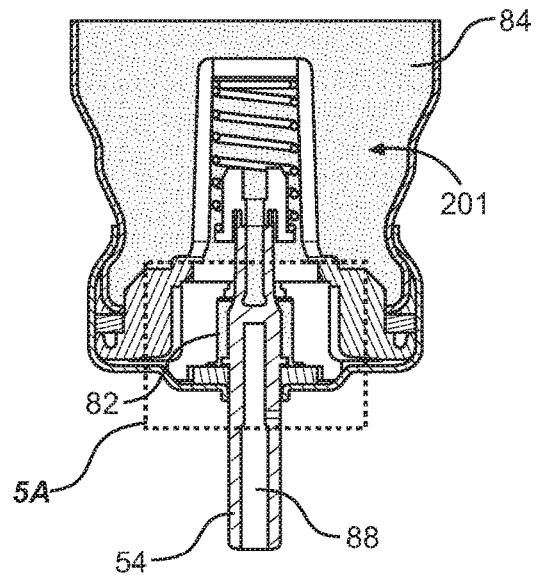


FIG. 5B

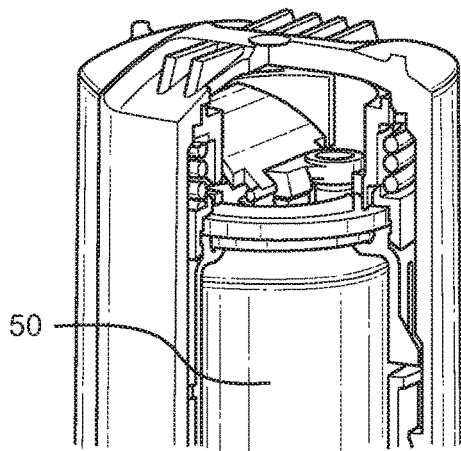


FIG. 5C

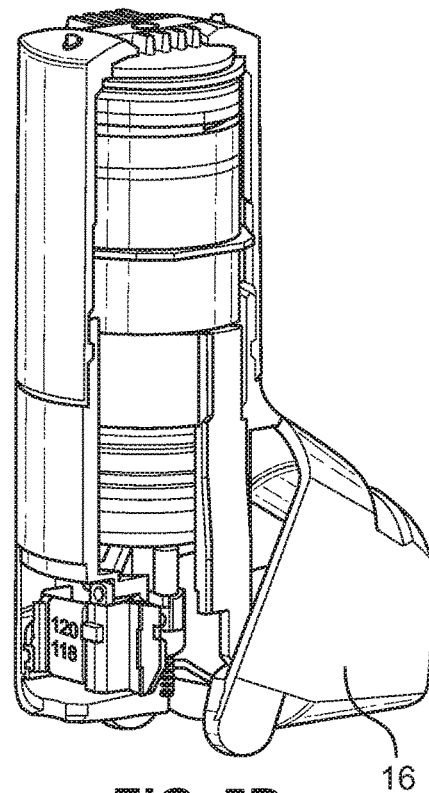


FIG. 5D

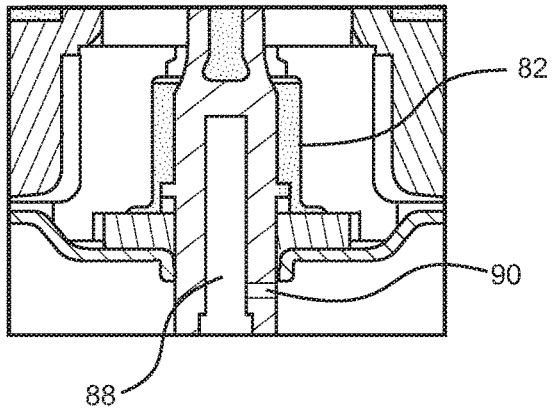


FIG. 6A

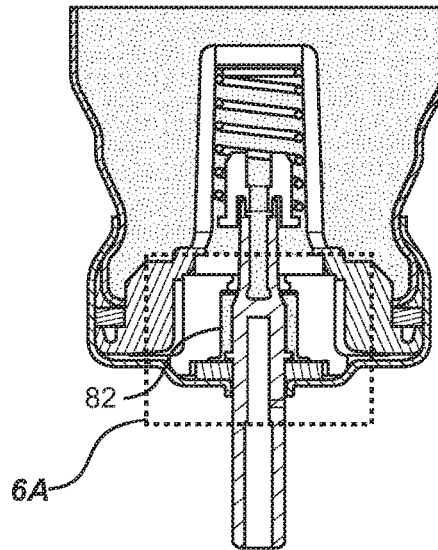


FIG. 6B

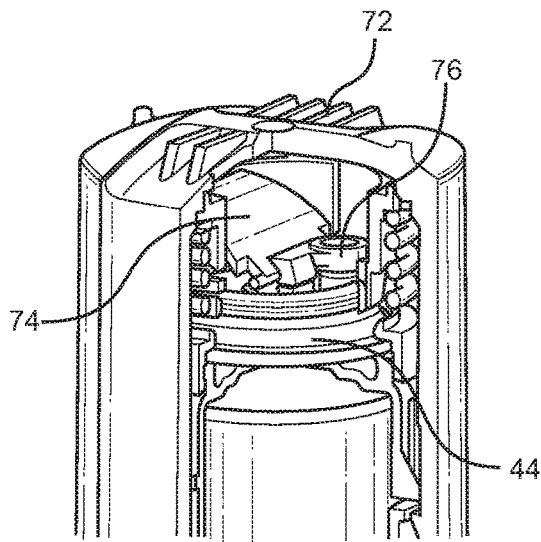


FIG. 6C

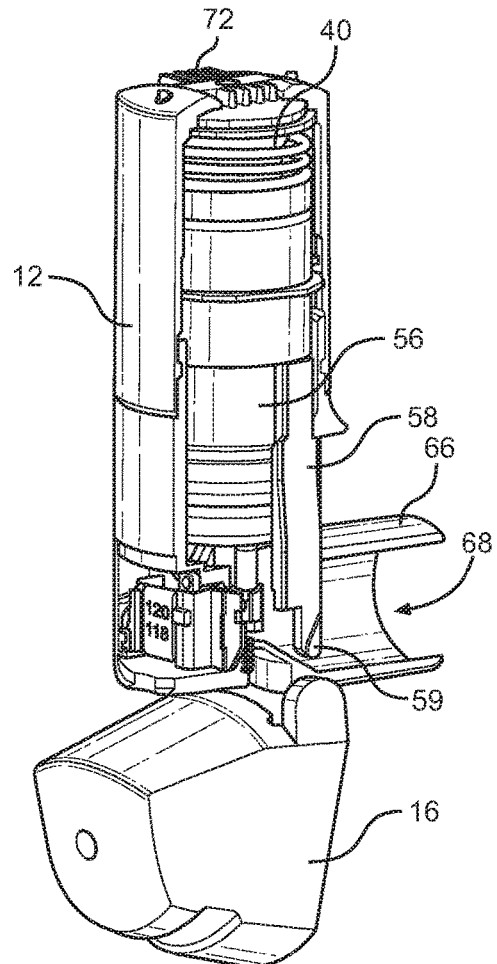


FIG. 6D

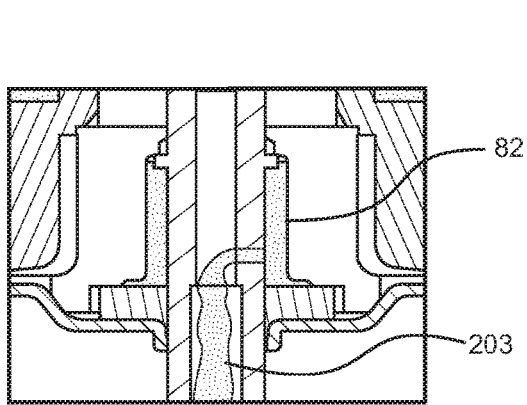


FIG. 7A

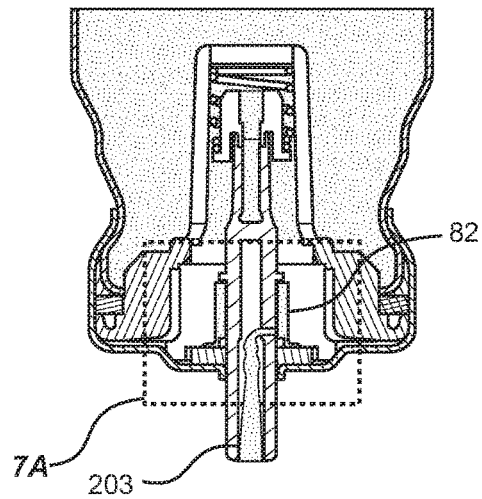


FIG. 7B

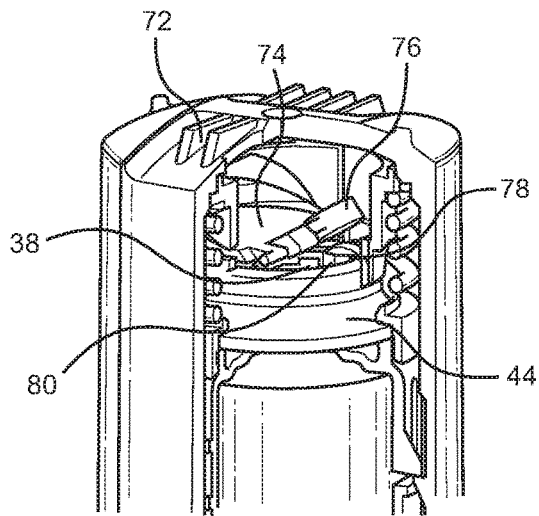


FIG. 7C

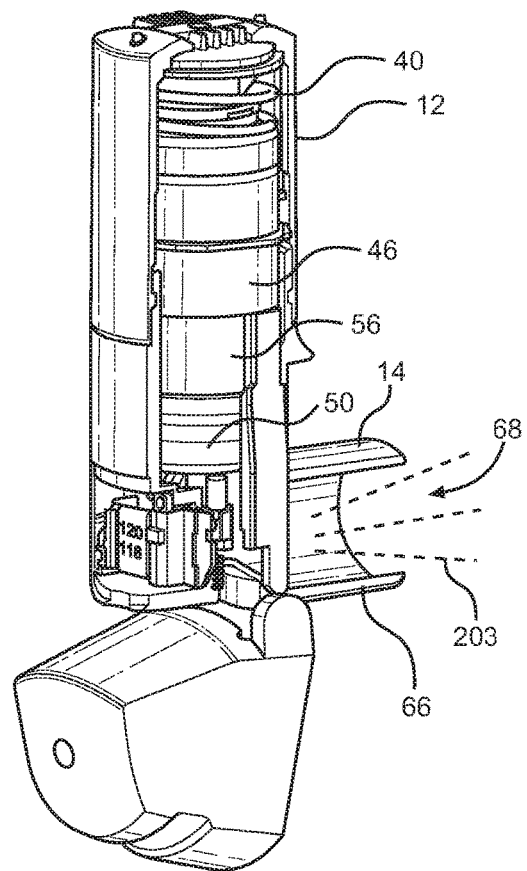


FIG. 7D

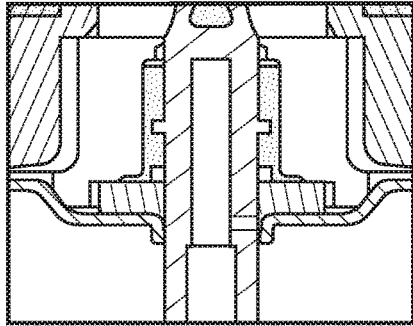


FIG. 8A

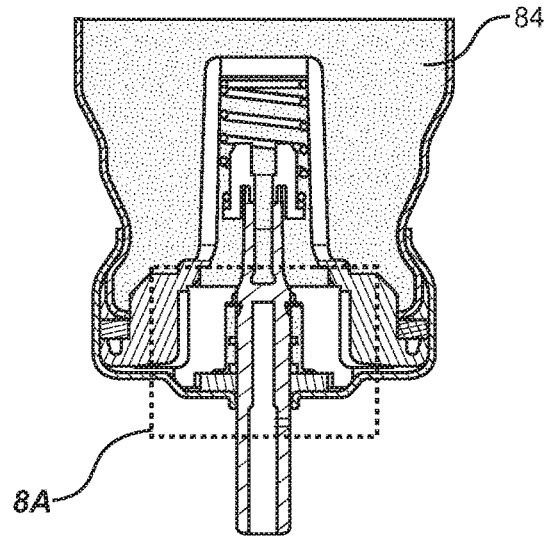


FIG. 8B

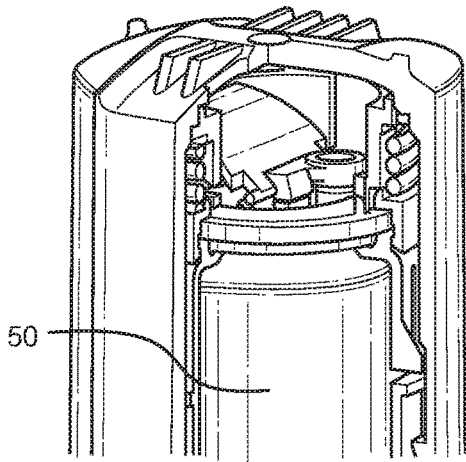


FIG. 8C

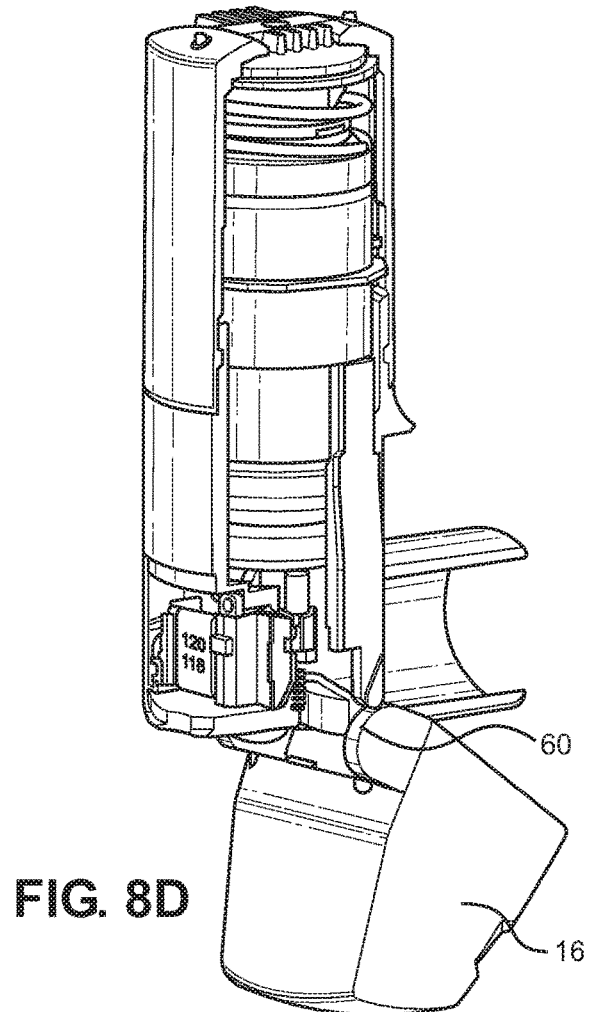
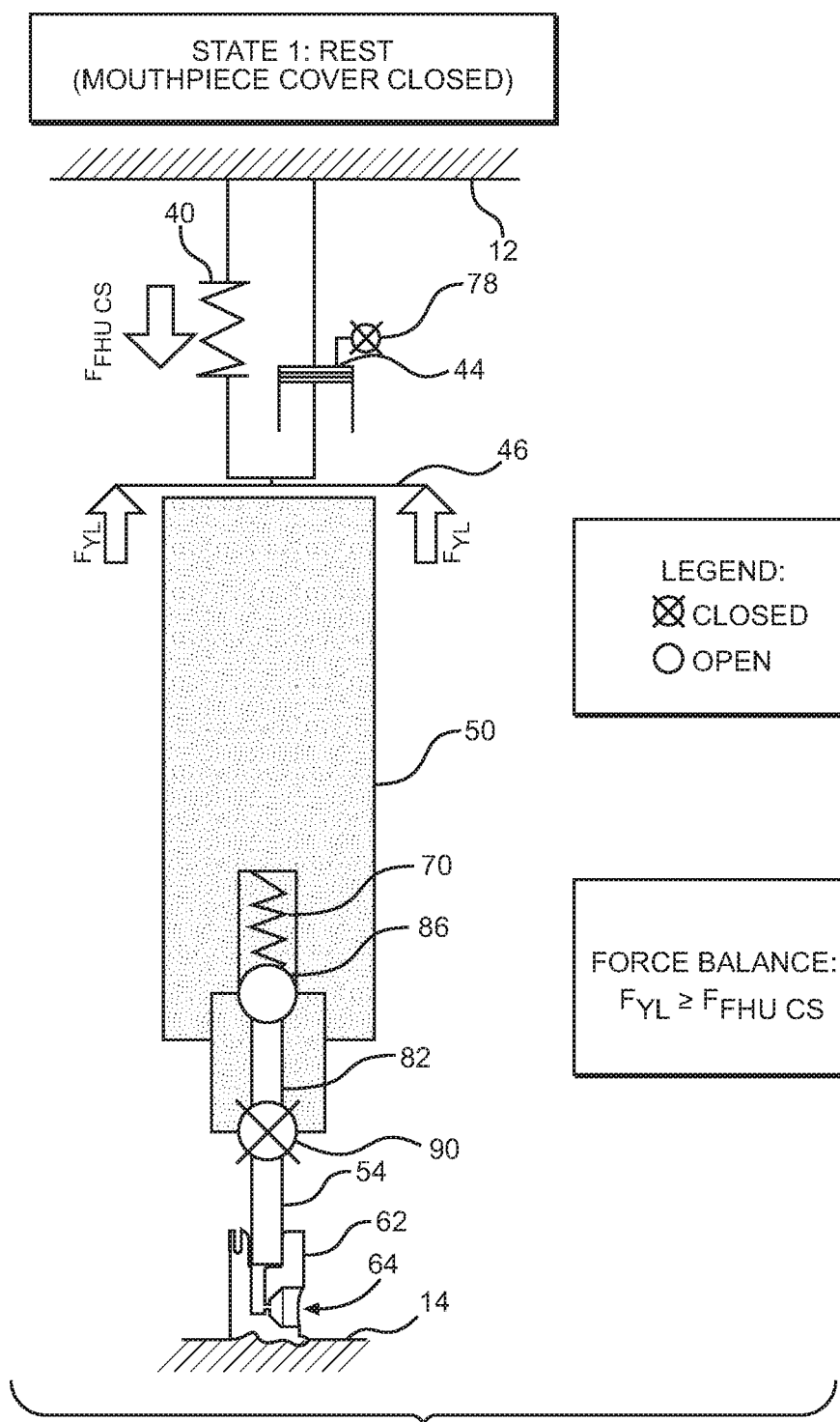
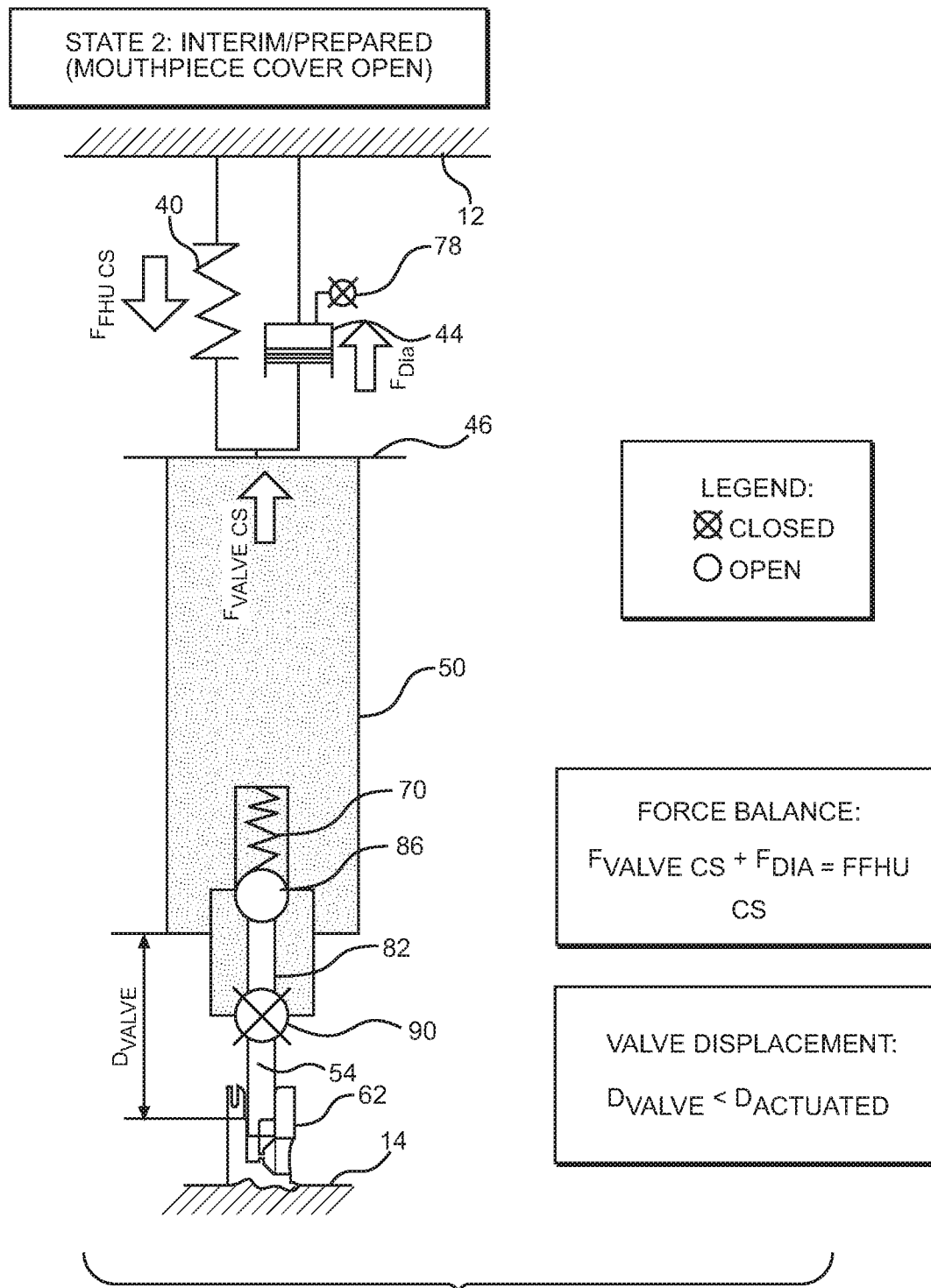
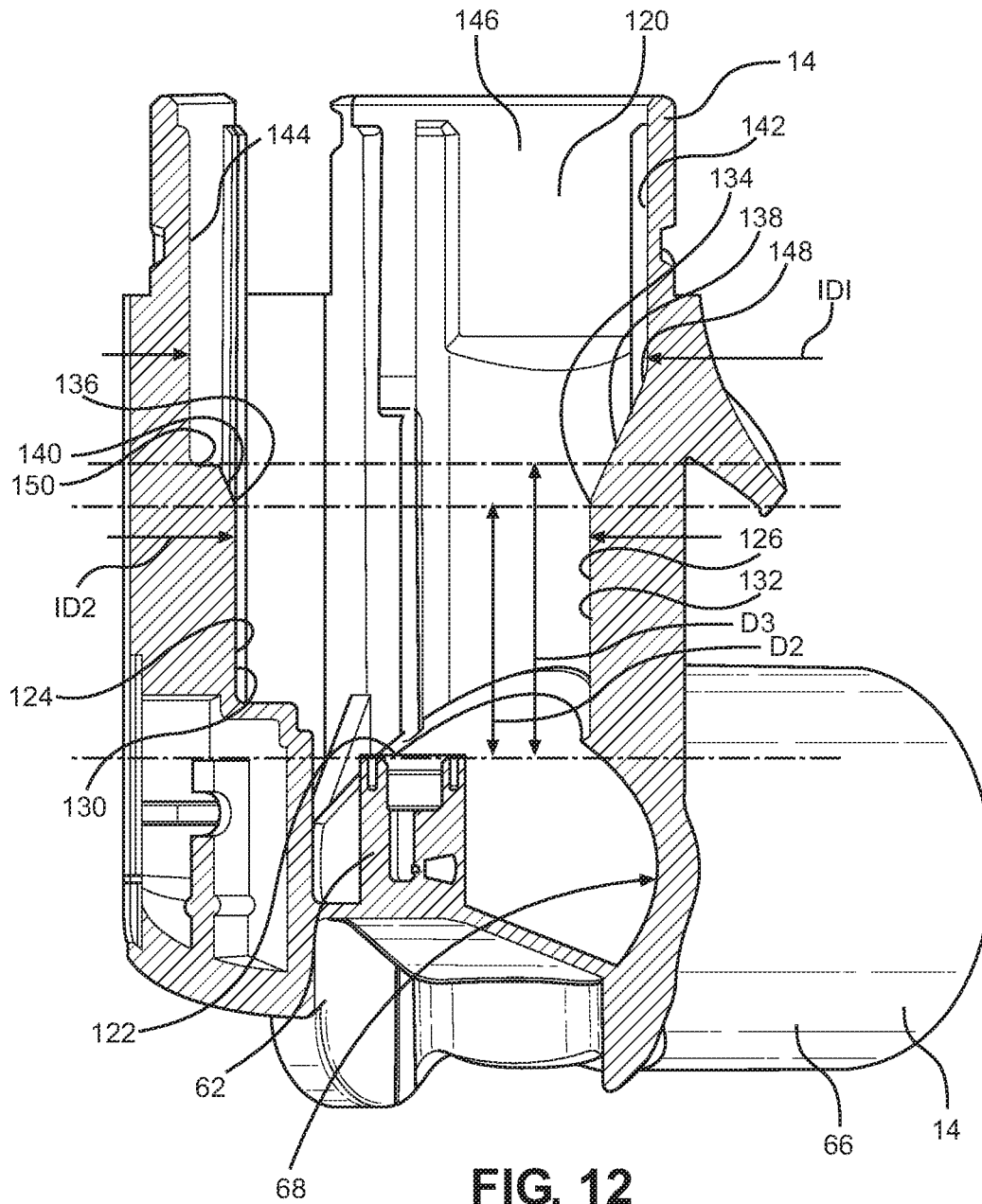


FIG. 8D









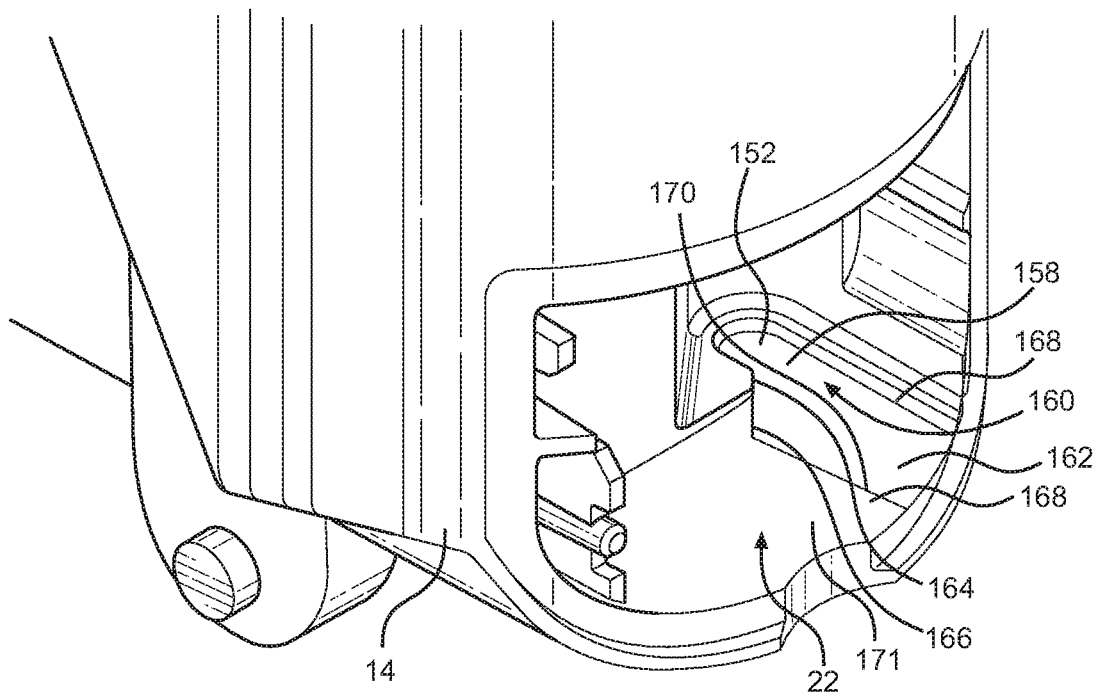
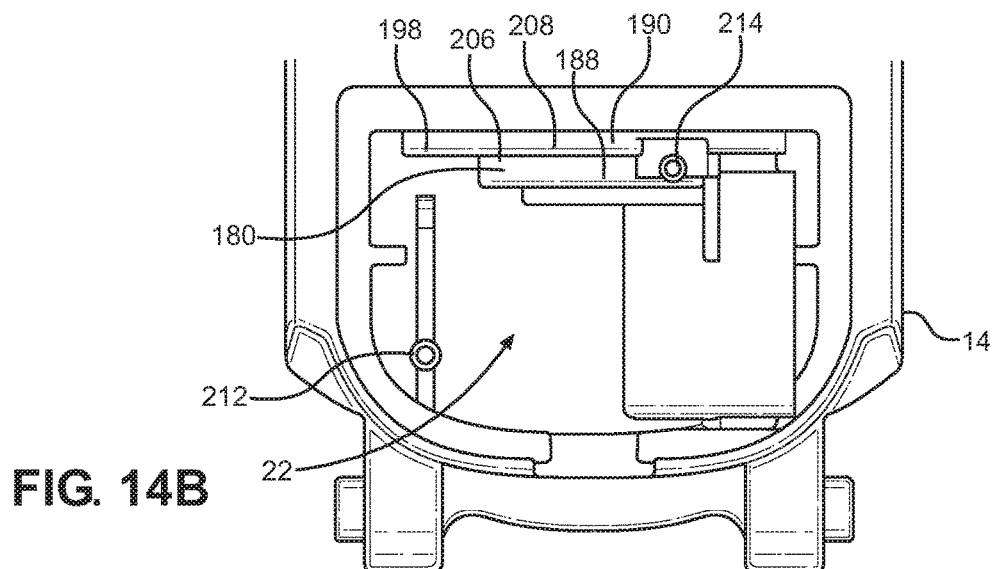
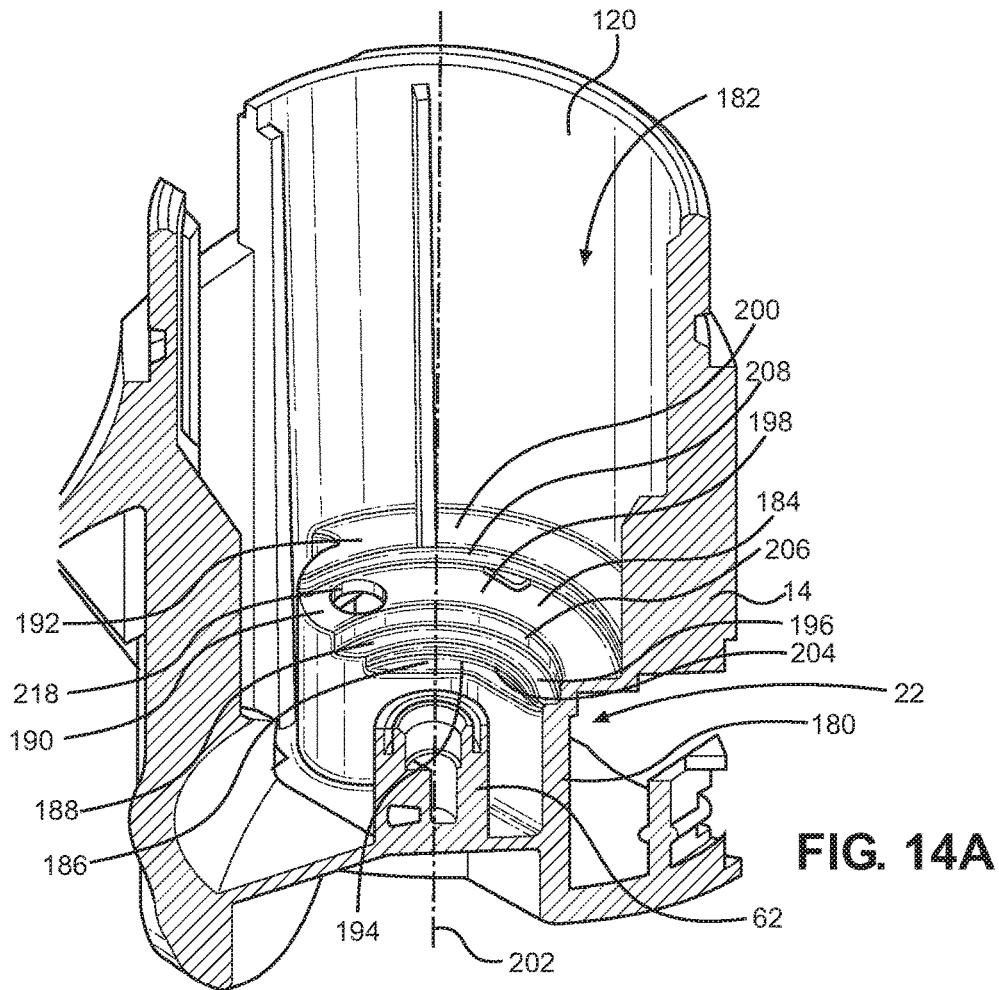


FIG. 13



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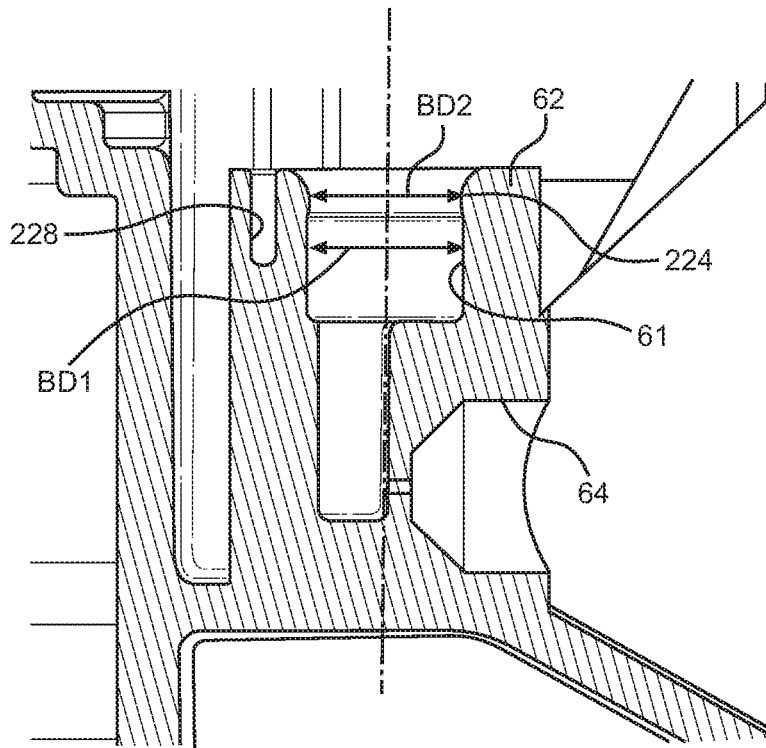


FIG. 15A

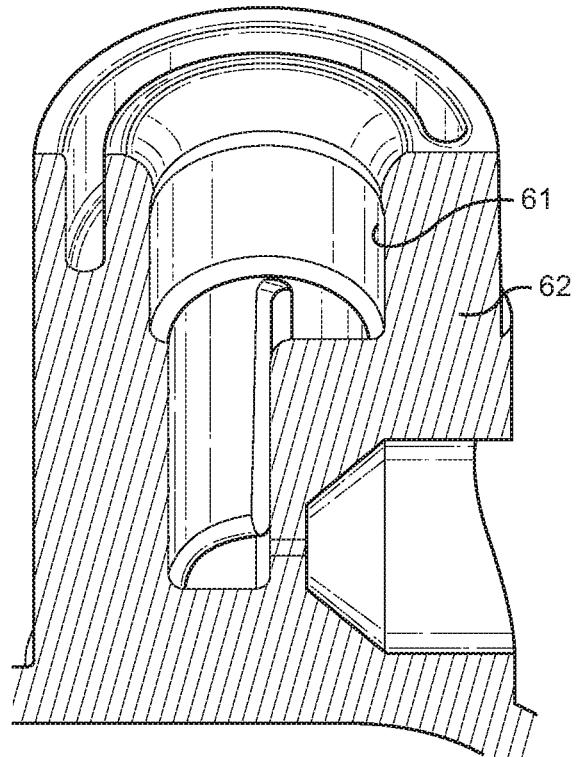


FIG. 15B

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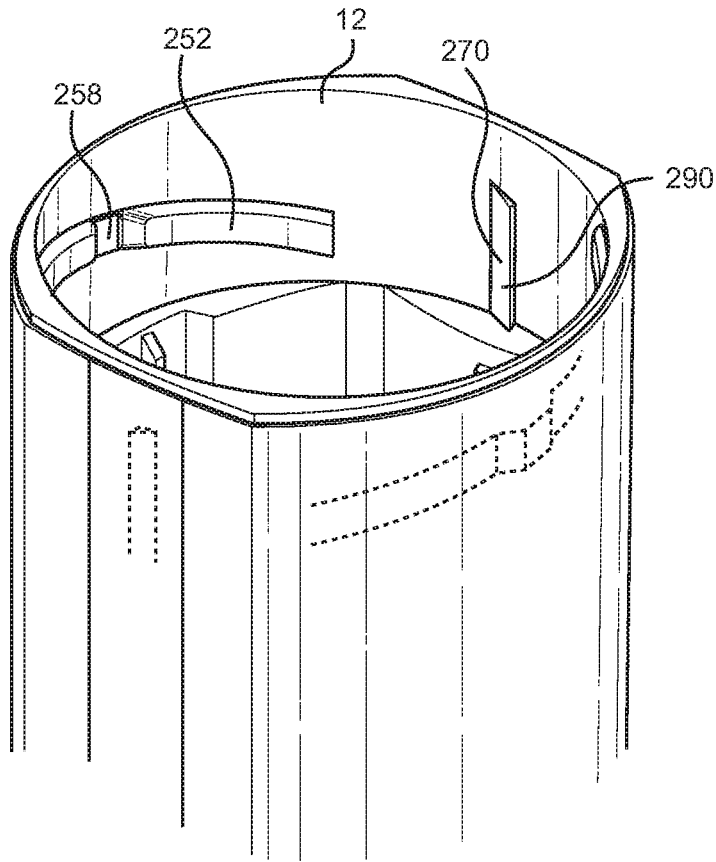


FIG. 16A

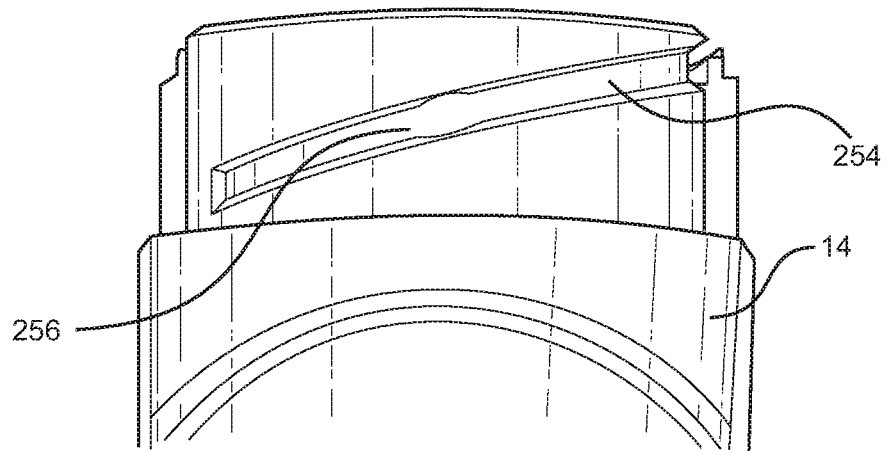


FIG. 16B

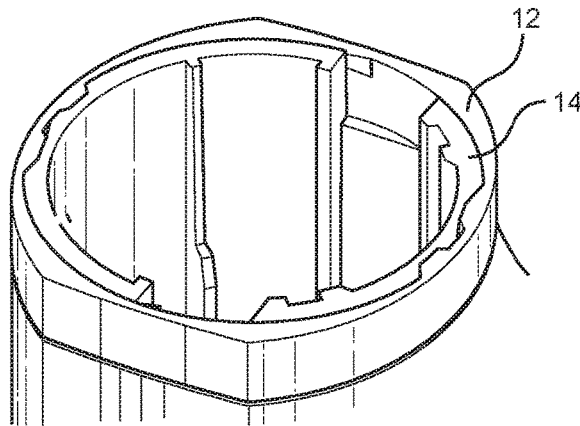


FIG. 17A

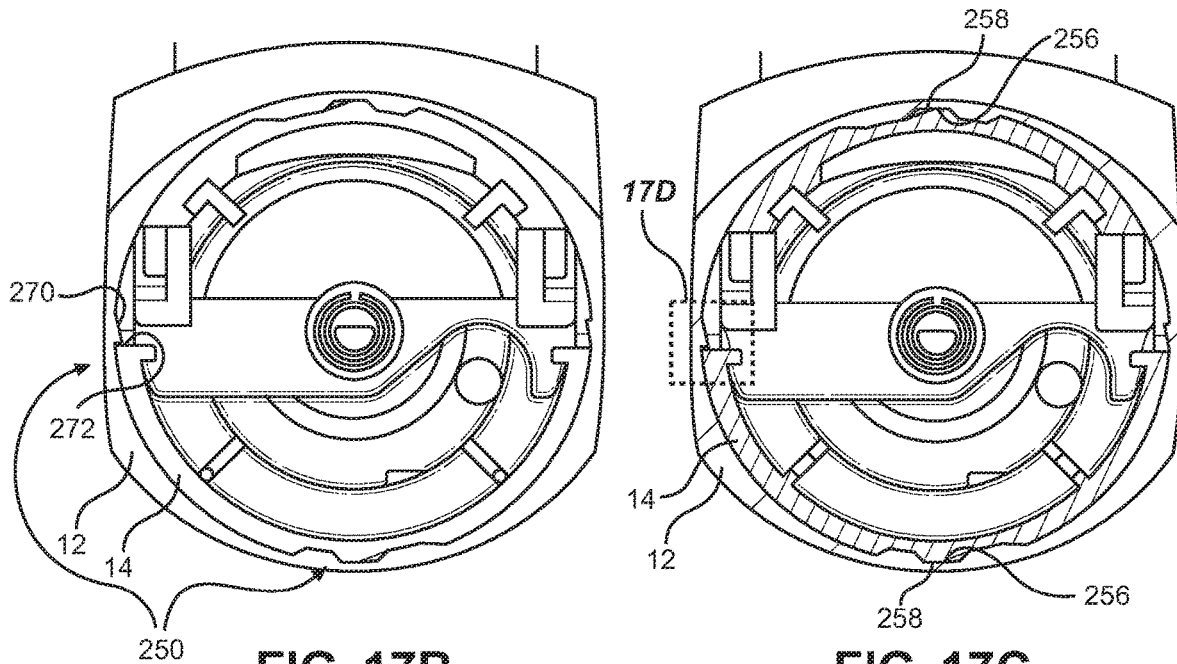


FIG. 17B

FIG. 17C

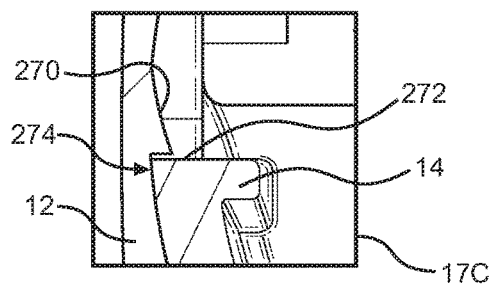


FIG. 17D

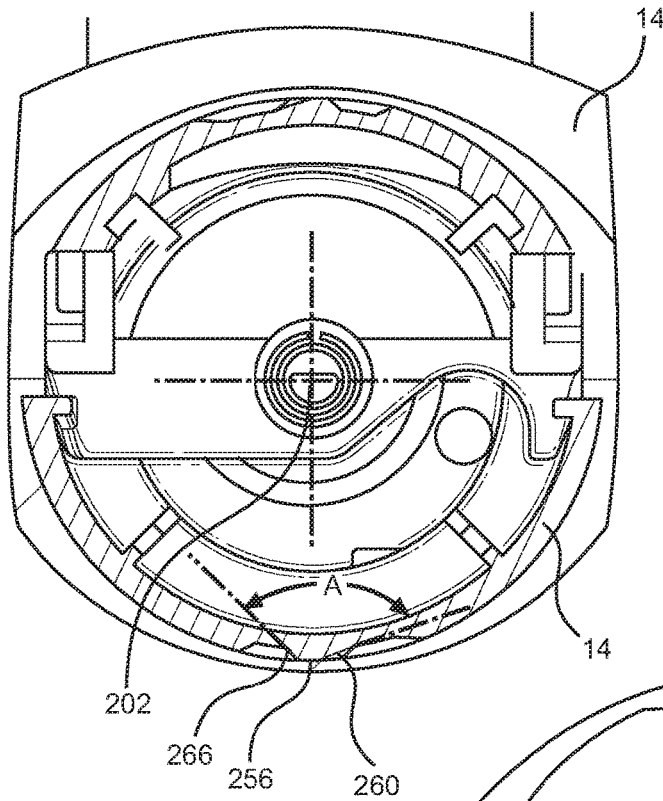


FIG. 18A

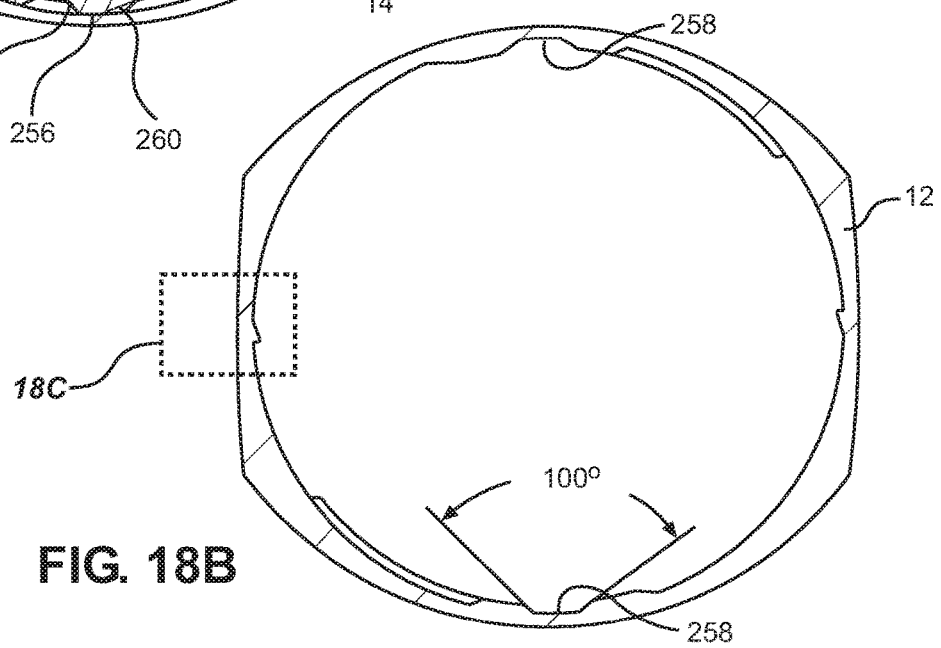


FIG. 18B

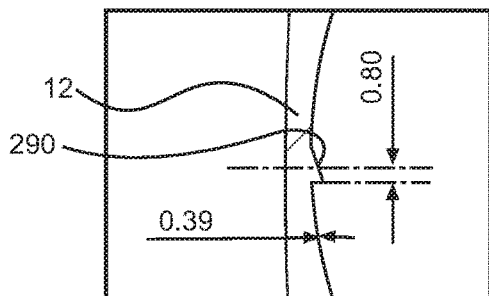
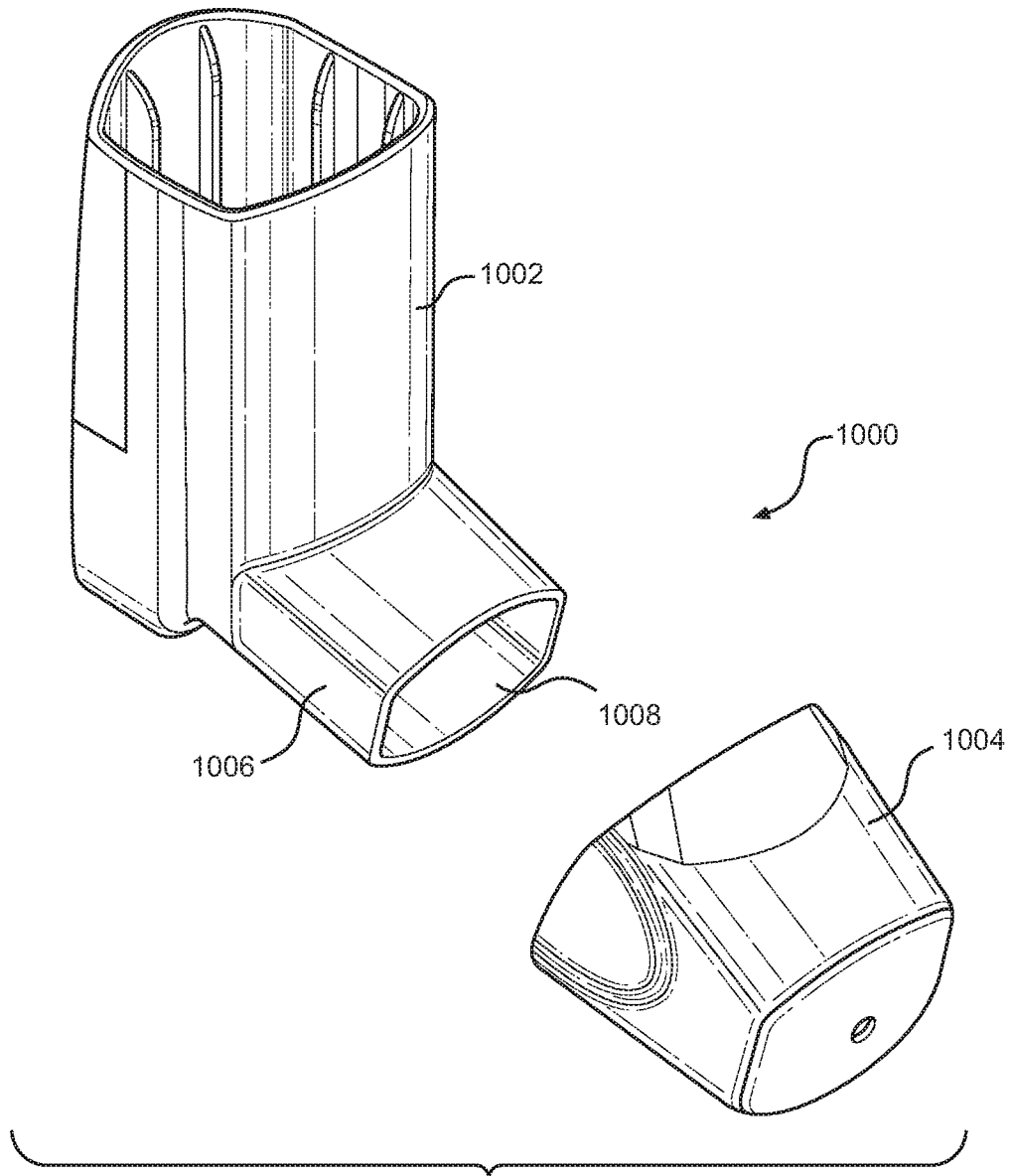


FIG. 18C



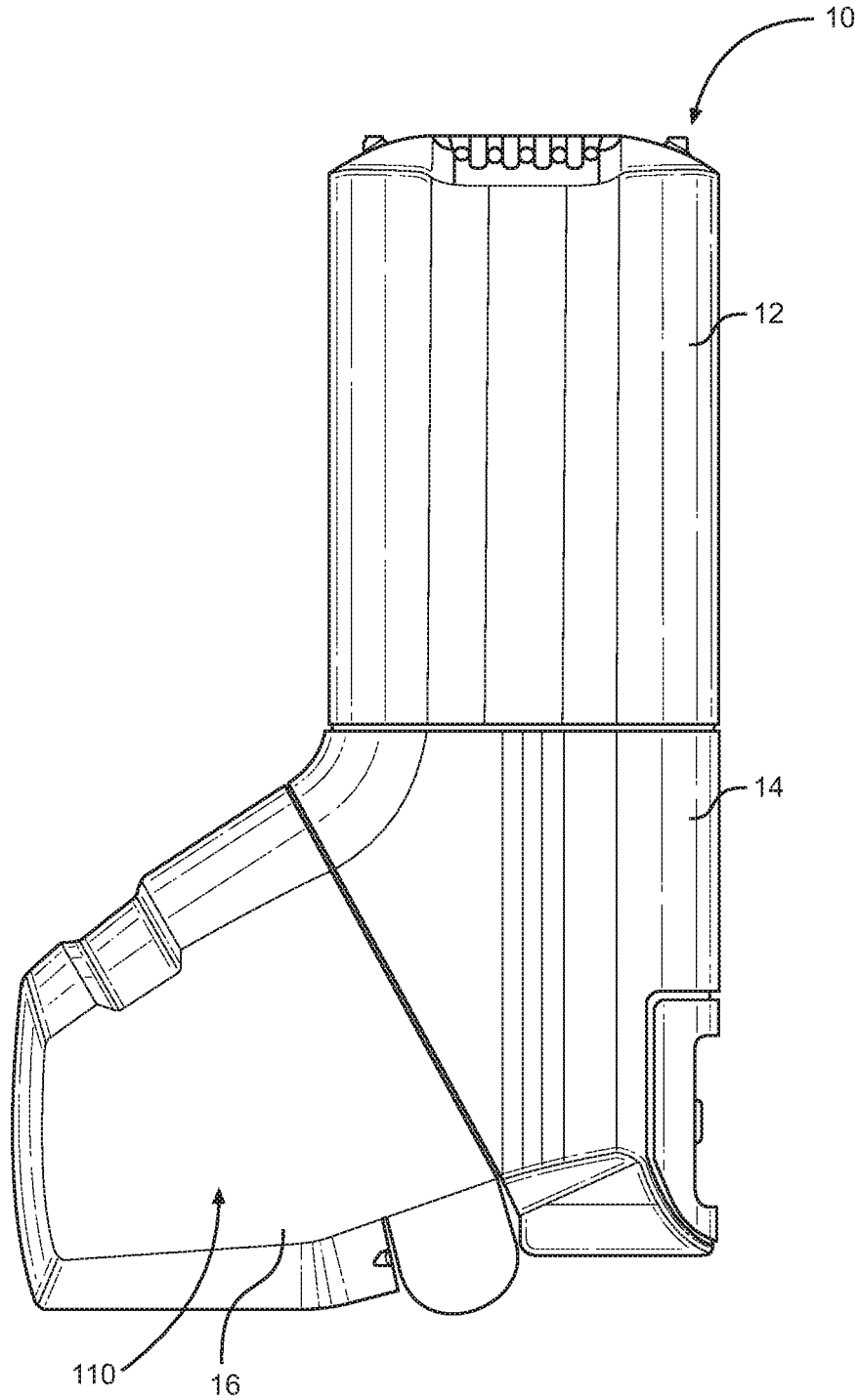


FIG. 20

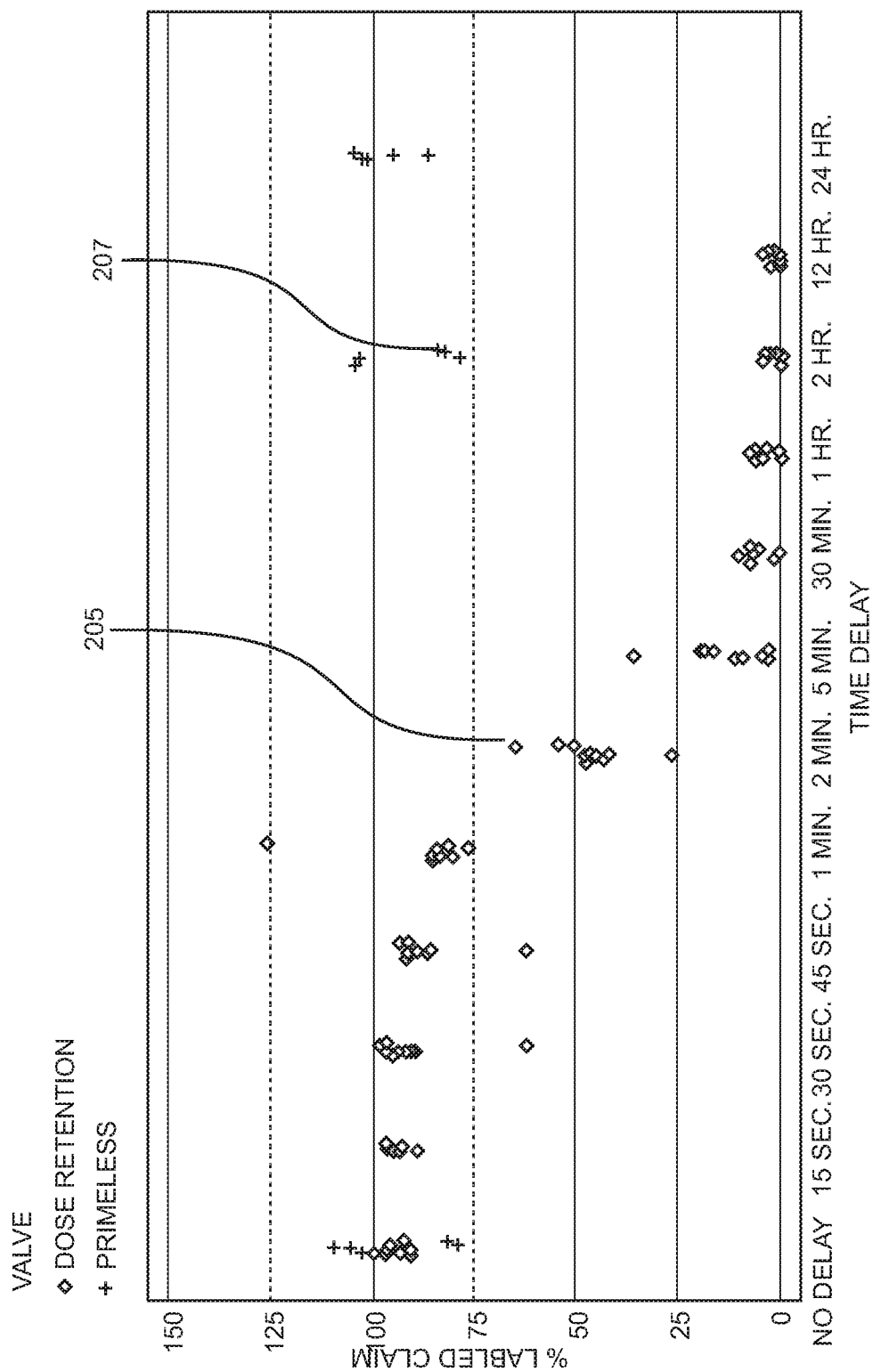


FIG. 21

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INHALERS AND RELATED METHODS

CROSS-REFERENCE TO RELATED
APPLICATIONS

This application is a continuation of U.S. patent application Ser. No. 15/881,283, filed Jan. 26, 2018, which claims the benefit of priority of Application No. GB1702407.6, filed Feb. 14, 2017, which applications are incorporated by reference herein, in their entireties and for all purposes.

FIELD OF THE INVENTION

The present invention relates to inhalers, including breath actuated and metered dose inhalers. The invention relates to oral and nasal inhalers. The invention also relates to methods of metering inhalable substances in metering valves of canisters for medicament inhalers, inhaler housings and inhaler valve stem and valve stem block interfaces.

BACKGROUND OF THE INVENTION

A known inhaler, which is a breath actuated inhaler, has a pressurised canister and a metering valve for controlling the ejection of inhalable substances from the canister. The canister is operable by a force holding unit having a cap housing attachable to a main housing of the inhaler. The metering valve includes a valve stem for transferring substances from an interior reservoir of the canister into the metering chamber and then out of the metering chamber along the valve stem in the direction of a nozzle of the inhaler. A radially directed capillary port is provided in the valve stem for communicating substances out of the interior reservoir for communication along the valve stem to the metering chamber and a similar port is provided for communicating substances out of the metering chamber and along the valve stem towards the nozzle. In use, a mouthpiece cap is opened to ready the inhaler for inhalation and then after inhalation the mouthpiece cap is closed and resets a canister fire system. It has been found that the inhaler can be left after inhalation with the mouthpiece dust cap in the opened position with the metering chamber communicating with atmosphere via the valve stem and nozzle. This can result in the variance of active ingredients in at least one subsequent dose. This means that users will sometimes remove a force holding unit cap housing from the main body of the inhaler and try to ensure that the metering chamber is sufficiently primed by firing a number of doses and this is both wasteful and may result in damage to the inhaler.

In some inhalers, when it is necessary to make changes to internal components, it is difficult to provide space and good guidance for all the necessary interior moving parts. Also, the assembly of some inhaler dose counters can be difficult.

Furthermore, in some inhalers, despite a tight connection between the valve stem and a valve stem block within the main body, blowback can occur which is leakage of substances between the valve stem block and valve stem. It can also be difficult in some inhalers to achieve reliable dose counting to reflect the number of doses actually provided by the inhaler.

The present invention aims to alleviate at least to a certain extent at least one of the problems of the prior art.

Alternatively, the present invention aims to provide a useful inhaler, method of metering substances in a metering valve of a canister for a medicament inhaler and/or useful inhaler parts.

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SUMMARY OF THE INVENTION

According to one aspect, the present disclosure discloses an inhaler housing for an inhaler for inhalable substances, the inhaler housing being arranged to contain a pressurised canister for sliding motion within a tubular body portion thereof, the inhaler housing having a valve stem block for connection to a valve stem of a pressurised canister, the valve stem block having a top surface, the tubular body portion having at least two mutually opposed guide ribs for guiding canister position within the tubular body portion, the guide ribs having substantially straight guide edges extending substantially parallel to and spaced from one another, each straight guide edge having an upper corner where the straight guide edge meets a further surface of the rib leading outwardly towards an upper rib section near an inner wall of the tubular body portion, at least one of the ribs having its straight guide edge's upper corner positioned a distance D2 in a direction parallel to an axis of the valve stem block along away from the top surface of the valve stem block, a distance between the straight guide edges of the ribs perpendicular to the axis being ID2, and in which the ratio D2/ID2 is less than 0.8.

It has been surprisingly found that ratios below this value enable very efficient and smooth guidance of the canister relative to the inhaler housing in some configurations.

The ratio D2/ID2 may be less than 0.75, about 0.7 being one example.

The further surface of at least one guide rib may extend away from the valve stem block and terminate at a distance D3 from the top surface of the valve stem block in the direction parallel to the axis, the ratio D3/ID2 being less than 0.9 or less than 0.85, about 0.8 being one example.

Each guide rib meets the upper rib section near the inner wall of the tubular body portion at outer rib positions wherein the outer rib positions are a distance ID1 apart in a direction perpendicular to the axis, and in which the ratio ID2/ID1 is between 0.7 and 0.9, typically between 0.75 and 0.85, about 0.78 or 0.8 being two examples.

According to a further aspect, the present disclosure discloses an inhaler housing for an inhaler for inhaling inhalable substances, the inhaler having: a body and a dose counter with an actuation member adapted to drive a dose indication portion of the dose counter against a return spring, the body including a recess for location of an end of the return spring; the recess having a substantially flat reaction surface, a shoulder surface adjacent the reaction surface and an entrance mouth into the reaction surface; wherein a distinct guide surface is provided for guiding the end of the return spring into the recess, the distinct guide surface being wider than the entrance mouth in a direction across the mouth.

This feature of the distinct guide surface being wider than the entrance mouth advantageously assists in assembly of the dose counter into the inhaler since when the return spring is being fitted as part of the dose counter installation it can slide along the distinct guide surface relatively easy into the recess.

The entrance mouth may have at least one chamfered entrance lip, the distinct guide surface having a slanted edge which is an extension of the lip.

The distinct guide surface may be substantially planar. The distinct guide surface may have an edge which intersects with an adjacent curved surface of the body.

At least a portion of the distinct guide surface may comprise a portion of the body which is recessed relative to an adjacent portion of the body.

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A further aspect of the present disclosure discloses an inhaler housing for an inhaler for inhaling inhalable substances, the inhaler housing having a tubular portion defining a tubular interior space for containing a pressurised canister containing inhaler substances, a valve stem block for engagement with a valve stem of such a pressurised canister, and a dose counter chamber for containing a dose counter assembly, the dose counter chamber being separated from the tubular interior space by a barrier, the barrier including a stepped upper wall area including at least three steps at different levels.

This configuration advantageously permits enough room for the dose counter in the dose counter chamber and enough room for the movable parts inside the inhaler housing including the pressurised canister and in at least one arrangement has been found to be particularly effective in space saving.

The inhaler may include four said steps.

The steps may be arcuate.

The arcuate steps may have substantially flat areas aligned substantially perpendicular to an axis of the valve stem block as well as part-cylindrical riser surfaces between the substantially flat areas.

The steps may be substantially concentric with an axis of the valve stem block.

The steps may extend around the valve stem block a distance of about 180 degrees.

The material forming the barrier may be of substantially constant thickness substantially throughout the steps.

The dose counter chamber may be formed with at least one heat staking pin for mounting of a dose counter system, the heat staking pin being directly attached to at least two of the steps.

The heat staking pin may be attached to at least one step surface that is oriented substantially perpendicular to an axis of the valve stem block and to at least one and preferably two step risers.

An aperture for a drive pin for actuating the dose counter may be formed through a second furthest step away from the valve stem block.

According to a further aspect, the present disclosure discloses an inhaler valve stem and valve stem block interface for a breath actuated inhaler having a dose counter, a pressurised canister containing inhaler substances including a medicament, which may be in solution or suspension, the valve stem block having a cylindrical inner bore with an inner diameter which is a first diameter, the cylindrical inner bore being for accepting a valve stem with an outer diameter, the valve stem block having a seal in the inner bore with a second diameter which is smaller than the first diameter.

It has been found with this configuration that, surprisingly, better sealing is achieved than with a simple interference fit between a cylindrical outer wall of a valve stem and a cylindrical inner wall of a valve stem block with a larger interference fit. This new configuration has been found to be particularly effective at sealing and avoiding blowback leakage. Especially with regard to the dose counter, the seal permits a relatively low insertion force to be needed to insert the valve stem into the valve stem block and enables very accurate positioning of the valve stem relative to the valve stem block in an axial direction of the valve stem, while at the same time providing a surprisingly effective seal bearing in mind the low insertion force.

The first diameter may be about 3.22 mm.

The first diameter may be about 3.5% larger than the second diameter.

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An outer diameter of the valve stem may be smaller than the first diameter but larger than the second diameter prior to introduction of the valve stem into the inner bore, preferably about 0.75% to 1.5% larger, for example about 1% larger.

The valve stem block may include an annular recess concentric with and extending around the inner bore at least partially around the circumference thereof, the inner diameter of the annular recess being about 25 to 50% larger than the inner diameter of the cylindrical inner bore, for example about 40% larger.

The seal may be inwardly convex.

The seal may have an inner surface which is part of a toroid.

The seal may be located at or near an entrance to the inner bore.

The seal may be formed integrally with, e.g. of the same material as, the material defining the inner bore which may, for example, be moulded plastics.

A further aspect of the present disclosure discloses a breath actuated inhaler having a drive adapted to drive a pressurised canister so as to retract a metering valve stem into the canister to fire the canister, the canister being adapted to move during operation between 1 and 4 mm between end positions of its length of travel relative to the valve stem, the drive being arranged to apply a firing force of between 15 N and 60 N of force to the canister at a position of the canister relative to the valve stem at which the canister fires.

With this configuration of drive and canister travel, it has been surprisingly found possible to have very accurate and reliable firing of the canister, as well as accurate counting when a dose counter is provided. Furthermore, a long extent of travel of the canister to retract the valve stem can be provided to ensure that both count and fire very reliably occur.

The drive may comprise a drive spring.

The canister may be arranged to move between 1 and 3 mm between the end positions. In one example the movement between the end positions is 3 mm.

The drive may be adapted to provide the firing force as more than 40 N, preferably also less than 60 N.

The drive may be adapted to provide the firing force as more than 35 N.

The firing force may be greater than the sum at the point of firing of opposing forces applied to the canister by a valve stem spring in the canister and a return spring for an actuator pin of a dose counter of the inhaler.

A further aspect of the present disclosure discloses a breath actuated inhaler having a main body for accommodating a medicament reservoir, a canister fire system for moving the canister to release a dose in response to air flow, a cap housing for enclosing the canister fire system and canister within an interior chamber defined by the main body and the cap housing, wherein a lock system is provided for locking the cap housing on the main body.

Advantageously, a user can be prevented from tampering with and damaging the interior components of the inhaler. In the case of a breath actuated inhaler, this is particularly advantageous because prior inhalers have required the ability to remove the cap housing for manual priming of the metering chamber. But, when a metering valve is provided with an opening configured to permit flow in a direction with an axial component along the valve stem directly between the transfer space inside the valve stem and the interior reservoir, and when the interior reservoir is arranged for orientation above the metering chamber whereby gas such as

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air located within the metering chamber is replaced with liquid from the interior reservoir, it is no longer necessary to be able to open the inhaler for manual priming of the metering chamber by manually pushing and firing the canister.

Helical threads may be provided for rotational attachment of the cap housing on the main body and for resisting relative longitudinal movement therebetween without rotation.

The lock system may include a protrusion in the region of a helical thread on one of the main body and the cap housing which is lockable in a recess in the region of a helical thread on the other of the main body and the cap housing.

Two said protrusions may be engageable in two said recesses formed at opposing locations on the inhaler.

Each protrusion may have a leading ramp surface and a trailing ramp surface, the included angle between the ramp and trailing surfaces being about 95° to 120°; the included angle of the protrusion preferably being larger than that of the recess.

The main body may have a central axis and the ramp surfaces are inclined at an angle of about 45° plus or minus 15° (or plus or minus 10°) to tangential.

The lock system may include a first lock member on one of the main body and the cap housing which is adapted to engage a second lock member at a lock interface formed by respective engagement faces thereof, the lock interface being oriented substantially perpendicular to tangential.

The main body may have a central axis and the first lock member has a radial extent of 0.25 to 0.75 mm, preferably about 0.35 to 0.45 mm; the first lock member preferably having a longitudinal extent of about 10 mm.

The main body and the cap housing may be formed of plastics material and the lock system may be configured so that a release torque required to overcome the locking provided by the plastics main body and cap housing is more than 1 Nm.

The lock system may be configured such that the release torque is between 2 and 5 Nm, preferably between 2.5 and 3 Nm, about 2.7 Nm being one example.

The present disclosure discloses in another aspect a method of metering inhalable substances in a metering valve of a canister for a medicament inhaler, the method comprising: providing the metering valve with a metering chamber and valve stem extending from a metering chamber to an interior reservoir of the canister, with the valve stem defining a communication path between the metering chamber and the interior reservoir, the communication path including an opening configured to permit flow between a transfer space inside the valve stem and the interior reservoir; and orienting the interior reservoir above the metering chamber and replacing gas such as air located within the metering chamber with liquid from the interior reservoir.

The present inventors have worked out that the reasons why inaccurate dosing can occur include that when the metering chamber is left vented to atmosphere in some prior inhalers for as little as 2 minutes, a gas or air lock can form in the metering chamber and when the metering chamber is next connected for communication with the interior reservoir, due to the radial capillary port, the gas or air is trapped within the metering chamber and liquid does not enter the metering chamber reliably as the next dose. The air may enter the metering chamber from the atmosphere in the prior art. This may happen as propellant in the metering chamber evaporates and diffuses into the atmosphere. Using the presently disclosed method which involves the use of the opening configured to permit flow in a direction with an

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axial component along the valve stem directly between a transfer space inside the valve stem and the interior reservoir, when the interior reservoir is oriented above the metering chamber, this enables liquid from the interior reservoir to replace gas such as air located within the metering chamber and an accurate dose can be administered at the next dose.

The opening may be configured to permit flow in a direction with an axial component along the valve stem directly between the transfer space inside the valve stem and the interior reservoir.

The replacing gas located in the metering chamber with liquid from the interior reservoir may include flowing liquid under pressure through the opening, along the valve stem to a portion of the communication path communicating with the metering chamber.

The method may include flowing gas from the metering chamber, in a direction counter to a direction of liquid flow from the interior reservoir, along the communication path into the interior chamber.

The method may include providing the opening as an elongated opening.

The method may include providing a second opening to the communication path diametrically opposed to the first said opening.

The method may include providing the valve stem with at least one said opening into the interior reservoir as having an axially oriented opening portion which is oriented facing directly axially along a longitudinal axis of the valve stem into the interior reservoir, and which includes flowing liquid into the metering chamber via said axially oriented opening portion.

The method may include venting the metering chamber to atmosphere via a valve stem block and/or nozzle.

The method may include operating the metering valve and canister within a medicament inhaler and holding the valve stem depressed relative to the canister with the metering chamber vented to atmosphere so as at least partially to permit substances within the metering chamber to vaporise and to permit atmospheric air to enter the metering chamber.

Advantageously, the inhaler can be left for a long period such as 24 hours with the metering chamber communicating with atmosphere and then when the metering chamber is reconnected to the interior reservoir and the interior reservoir is oriented above the metering chamber the metering chamber can fully fill with liquid for the next dose. Advantageously, in a breath actuated inhaler, the features of the method mean therefore that any force holding unit and/or cap housing for the inhaler can be permanently secured or locked on to the inhaler so that users cannot tamper with the interior and there is no need to perform manual priming of the metering valve, which is a necessity in prior art inhalers, before the next dose is taken.

The method may include providing the medicament inhaler as a breath actuated inhaler, and may include, in response to air flow, firing the canister by closing communication between the metering chamber and interior reservoir and opening communication between the metering chamber and atmosphere, the valve stem being held depressed after firing.

The method may include resetting the inhaler to a reset configuration with a reset actuator so as to close communication between the metering chamber and atmosphere and open communication between the metering chamber and the interior reservoir, and carrying out the orienting of the interior reservoir above the metering chamber while the inhaler is in the reset configuration.

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The method may include providing the reset actuator as a lever, press button, hinged or rotatable piece, dust cap, nasal outlet cap or mouthpiece cap for the inhaler. Closing the actuator may reset the inhaler. In the case of an oral inhaler the reset actuator may be a dust cap mouthpiece cap. In the case of a nasal inhaler, the reset actuator may take a variety of forms, including but not limited to a dust cap or a movable lever, cap or button. In this case, the carrying out of the orienting of the interior reservoir above the metering chamber being carried out once the reset actuator has been opened to a configuration suitable for inhalation or otherwise operated. Therefore, it can be ensured that right before inhalation, the metering chamber is full of liquid and any gas which may have been in the metering chamber has been drawn into the interior reservoir due to the free flowing communication pathway between metering chamber and interior reservoir.

In an alternative embodiment, the inhaler may include a dust cap or mouthpiece cap which closes communication between the metering chamber and atmosphere but does not reset the inhaler. In these cases, optionally, a separate reset actuator may be provided.

The method may include providing the medicament inhaler as a metered dose inhaler and may include applying a force to the canister to hold the valve stem depressed; and may include subsequently releasing the canister to extend the valve stem and carrying out the orienting of the interior reservoir above the metering chamber.

The method may include providing the inhalable substances as including at least one propellant.

The method may include providing at least one said propellant as a hydrofluoroalkane, such as 1,1,1,2-tetrafluoroethane.

The method may include providing at least one said propellant with a surface tension at 25° C. of about 6 to 10 mN/m, typically about 7 to 9 mN/m, about 8 mN/m being one example.

Advantageously, it has been found that fluid with this surface tension is capable of avoiding gas or air lock in the metering chamber by flowing into the metering chamber when the features of the presently disclosed method are used.

The method may include providing the inhalable substances as including an active ingredient in suspension or in solution, such as beclomethasone dipropionate (BDP) or tiotropium bromide.

The present disclosure also discloses in another aspect a breath actuated inhaler for the inhalation of inhalable substances, the inhaler comprising: a canister having an interior reservoir containing pressurised inhalable substances including fluid; a metering valve including a metering chamber and a valve stem defining a communication path between the metering chamber and the interior reservoir, the communication path including an opening configured to permit flow between a transfer space inside the valve stem and the interior reservoir, the interior reservoir being arranged for orientation above the metering chamber whereby gas such as air located within the metering chamber is replaced with liquid from the interior reservoir.

Advantageously, with this configuration of metering valve there is no need to manually prime the metering chamber by repeatedly firing the canister manually and an accurate next dose can be provided to the metering chamber since a gas or air lock can be avoided. This also means, advantageously, that in a breath actuated inhaler having a force holding unit or cap housing secured to a main body of the inhaler, these components may be locked together so that it is relatively

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difficult for a user to remove the force holding unit or cap housing and tamper with the interior components. Instead, there is no need to perform manual priming and the inhaler main housing and the cap housing can be permanently locked together enclosing the internal moving parts of the inhaler where they cannot easily be damaged.

The opening may be configured to permit flow in a direction with an axial component along the valve stem directly between a transfer space inside the valve stem and the interior reservoir.

The communication path may be configured to permit liquid to flow under pressure along the communication path to the metering chamber and gas to flow in a reverse direction therealong from the metering chamber into the interior reservoir.

The opening may comprise an elongated opening.

The inhaler may include a second opening or further openings into the communication path.

The second opening may be diametrically opposed to the first said opening.

The valve stem may have at least one opening into the interior reservoir with an axially oriented portion facing directly axially along a longitudinal axis of the valve stem into the interior reservoir for the flow of fluid directly into the communication path in an axial direction along the valve stem.

The inhaler may include a metering chamber exit port for venting the metering chamber to atmosphere via a stem block and/or nozzle.

The inhaler may include a canister fire system for ejecting inhalable substances from the inhaler in response to air flow by closing communication between the metering chamber and the interior reservoir and opening communication between the metering chamber and atmosphere. The canister fire system preferably includes a drive such as a spring for driving the canister relative to the valve stem. The inhaler may have an actuator system for operating the drive, the actuator system optionally including a vacuum chamber having a vacuum release system operable to permit the drive to drive movement of the canister relative to the valve stem. The vacuum release system may be air flow actuatable.

The actuator and/or drive may include or operate as a latch, trigger or switch and may take other forms in other embodiments such as being electromechanical.

The canister fire system may be adapted to depress the valve stem into the canister to cause inhalable substances to be ejected from the inhaler and to hold the valve stem depressed with the metering chamber communicating with atmosphere.

The canister fire system may include a reset actuator which is operable so as to extend the valve stem relative to the canister in order to close communication between atmosphere and the metering chamber and to open communication between the metering chamber and the interior reservoir.

In the case of a nasal inhaler, the reset actuator may, for example, comprise a dust cap or a lever, cap or button. In the case of an oral inhaler, the reset actuator may comprise a dust cap or mouthpiece cap for a mouthpiece of the inhaler. The mouthpiece cap may be closable to permit extension of the valve stem relative to the canister, the mouthpiece cap optionally being hingedly connected to a main housing of the inhaler for camming engagement with at least one drive rod. The drive rod may be associated with a yoke for pushing on a drive element to compress a spring of the drive.

In an alternative embodiment, the inhaler may include a dust cap or mouthpiece cap which closes communication

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between the metering chamber and atmosphere but does not reset the inhaler. In these cases, optionally, a separate reset actuator may be provided.

The inhaler may include a preventer adapted, after an inhalation has taken place, to prevent a further inhalation until the reset actuator has been operated to extend the valve stem. In the case of a mouthpiece or other cap, this may comprise closing the cap.

Advantageously, the preventer may therefore ensure that the user closes the cap at some time before each inhalation and this in turn means that reliable dosing can be achieved.

The preventer may comprise a warning signaller, such as an audible or visual alarm, dose counter or warning notice, quick reference guide or instructions.

The inhaler may include inhalable substances in the interior reservoir which include at least one propellant.

At least one said propellant may comprise a hydrofluoroalkane, such as 1,1,1,2-tetrafluoroethane.

At least one said propellant may have a surface tension at 25° C. of about 6 to 10 mN/m, typically about 7 to 9 mN/m, about 8 mN/m being on example.

The inhaler may include at least one inhalable substance in the interior reservoir as an active ingredient, for example in suspension or in solution, such as beclomethasone dipropionate or tiotropium bromide.

The inhaler may include a dose counter for counting doses, preferably for making one count with each inhalation of a dose.

The dose counter may include: (a) a tape bearing dose indicia for displaying counts and/or (b) an actuator pin for contact with the canister, or a body movable therewith, for counting doses, and preferably a dose counter chamber separated by a barrier from an inner space of the inhaler for containing the canister, the actuator pin optionally extending out of the dose counter chamber through an aperture in the wall for contact during counting with the canister (or the body movable therewith).

The inhaler may be a breath actuated inhaler.

The inhaler may be a metered dose inhaler.

The inhaler may be an oral inhaler.

The inhaler may be a nasal inhaler.

The inhaler may include a reset actuator which when actuated prevents exposure of the metering chamber to atmosphere, wherein the inhaler provides 75 to 125% of labelled claim for a dose following exposure of the metering chamber to atmosphere for a time period which is more than one minute.

In this case, the reset actuator may be a mouthpiece cap that, when closed, prevents exposure of the metering chamber to atmosphere.

The inhaler may provide 75 to 125% of labelled claim for a dose following exposure of the metering chamber to atmosphere for a time period which is more than two minutes.

The inhaler may provide 75 to 125% of labelled claim for a dose following exposure of the metering chamber to atmosphere for a time period which is one hour, more than one hour, 24 hours or more than 24 hours.

Operation of the inhaler may include, subsequent to closing the mouthpiece, opening the mouthpiece.

The inhaler may include a metering valve spring and an opposing canister spring for drivingly firing the canister, the metering valve spring, canister spring and metering valve being arranged in the inhaler such that an equilibrium of various forces is achieved in at least one ready-to-fire configuration of the inhaler.

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In that case, the operation of the inhaler may include at least one suction force, e.g. provided by a pneumatic chamber; the suction force preferably operating against the canister spring.

In another aspect, the present application discloses use of a metering valve for preventing gas lock within a metering chamber of an inhaler having a pressurised canister, the metering valve having a metering chamber and a valve stem extending from the metering chamber to an interior reservoir of the canister, with the valve stem defining a communication path between the metering chamber and the interior reservoir, the communication path including an opening configured to permit flow between a transfer space inside the valve stem and the interior reservoir, in use the interior reservoir being oriented above the metering chamber so as to cause movement through the opening and gas such as air located within the metering chamber to be replaced with liquid from the interior reservoir.

The use may be performed in a breath actuated inhaler. The inhaler may be oral. Nasal inhalers of this type are also envisaged.

The use may be performed in a metered dose inhaler. The metered dose inhaler may be oral or nasal.

When the present disclosure is implemented in a metered dose inhaler, this may comprise a press and breathe metered dose inhaler, for example in which a canister is pushed by hand to fire, normally directly although indirect operation is an alternative, normally using finger and/or thumb operation of the canister.

BRIEF DESCRIPTION OF THE DRAWINGS

The present invention may be carried out in various ways and a number of preferred embodiments will now be described by way of example with reference to the accompanying drawings, in which:

FIGS. 1A and 1B show respective isometric views of a preferred inhaler;

FIG. 2 shows an exploded view of the inhaler shown in FIGS. 1A and 1B;

FIG. 3 is an enlarged view of the dose counter assembly shown in FIG. 2;

FIG. 4 is an isometric sectional view of a metering valve of the inhaler and part of the canister shown in FIG. 2;

FIGS. 5A, 5B, 5C and 5D show various details of the inhaler and parts of it in a closed configuration thereof;

FIGS. 6A, 6B, 6C and 6D show various details of the inhaler in an opened configuration thereof;

FIGS. 7A, 7B, 7C and 7D show various details of the inhaler in an actuated configuration thereof;

FIGS. 8A, 8B, 8C and 8D show various details of the inhaler in a closing configuration thereof;

FIG. 9 schematically shows forces and ports within the inhaler in the closed configuration of FIGS. 5A to 5D;

FIG. 10 schematically shows forces and ports within the inhaler in the opened configuration of FIGS. 6A to 6D;

FIG. 11 schematically shows forces and ports within the inhaler in the actuated configuration of FIGS. 7A to 7D;

FIG. 12 is a sectional elevational view of part of the inhaler shown in FIG. 1A with long dash lines denoting the top of ribs used in an earlier prototype;

FIG. 13 shows a portion of the inhaler of FIG. 1A with the dose counter and dose counter door removed;

FIG. 14A is a sectional isometric view of part of the inhaler shown in FIG. 1A;

FIG. 14B shows part of the inhaler with a dose counter not yet installed, showing heat stake pins;

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FIGS. 15A and 15B show respective side elevation and isometric views of the valve stem block of the inhaler of FIG. 1A;

FIGS. 16A, 16B, 17A, 17B, 17C, 17D, 18A, 18B and 18C show various views of part of the inhaler, including components showing the interlocking interaction of the main body of the inhaler with a cap housing thereof;

FIG. 19 shows a modified form of the inhaler of FIG. 1A in which the force holding unit and cap housing are removed and the modified inhaler takes up the form of a metered dose inhaler; and

FIG. 20 shows a side view of the inhaler shown in FIG. 1A; and

FIG. 21 shows a comparative graph of delivered dose recovery at various time delays post previous actuation for the inhaler of FIG. 1A and an inhaler having a metering valve with radial capillary metering chamber inlet and outlet ports.

DETAILED DESCRIPTION OF THE INVENTION

The following detailed description of embodiments of the inhaler and accompanying methods will be better understood when read in conjunction with the appended drawings of exemplary embodiments. It should be understood, however, that the invention is not limited to the precise arrangements and instrumentalities described in the following detailed description.

As shown in FIGS. 1A and 1B, a breath actuated inhaler which is merely an example of an inhaler in accordance with the present invention, includes a force holding unit or cap housing 12, a main body 14, a mouthpiece dust cap 16 and a dose counter door 18 having a dose counter window 20.

As shown by the exploded view of FIG. 2, a dose counter chamber 22 includes a dose counter system 24 closed within it by the dose counter door 18.

The dose counter system is shown in enlarged detail in FIG. 3 and includes an actuating pin 26 and return spring 28. The dose counter can take various forms and may, for example, be as described in EP2135199A or EP2514464A.

As also shown in FIG. 2, the inhaler 10 includes a force holding unit 30 which includes: a filter 32, flap valve housing 34, flap valve 36, flap valve spring 38, main compression spring 40, retaining ring 42, diaphragm 44 and lower cap 46. The inhaler also includes a canister 50 with a metering valve 52 and a valve stem 54; as well as a yoke 56 with drive rods or legs 58 having distal ends 59 which are driven by respective cams 60 on the hingedly-connected mouthpiece dust cap. The valve stem 54 is fitted into an inner bore 61 (FIG. 15B) of a valve stem block 62 which communicates with a nozzle 64 for ejection of inhalable substances through a central bore 68 (FIG. 12) of a mouthpiece 66 (FIG. 12 and FIG. 2) of the main body 14 of the inhaler 10.

The force holding unit 30 operates substantially as disclosed with reference to FIGS. 1 to 3 of EP1289589A and the yoke 56 and mouthpiece dust cap 16 substantially as described in EP2514465A, including but not limited to FIG. 22 thereof.

In particular, with reference to FIGS. 5A to 5D, starting from a configuration in which the mouthpiece dust cap 16 is closed in this configuration the liquid 201 in an interior reservoir 84 of canister 50 communicates with a metering chamber 82 which does not communicate with atmosphere through an interior bore 88 of the valve stem 54. An opening rotation of the mouthpiece dust cap 16 to the configuration

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of FIGS. 6A to 6D enables the distal ends 59 of the drive rods 58 and indeed the whole yoke 56 to be moved away from the cap housing 12 under the influence of the main compression spring 40, the main compression spring 40 being reacted against as equilibrium is reached for the canister position by friction forces as well as forces provided by partial vacuum at the diaphragm, the dose counter return spring 28, and metering valve spring 70 (FIG. 4) which forms part of the metering valve 52. In this configuration, the metering chamber 82 is isolated from both of the interior reservoir 84 and atmosphere.

As the next step, the user (not shown) inhales through the mouthpiece 66 and the drawing out of air through the central bore 68 in turn draws air into the enclosure formed by the main body 14 and cap housing 12 through the series of approximately ten air inlets 72 formed on the cap housing 12. The incoming air impinges upon the flap 74 which releases vacuum (i.e. a partial vacuum) from the vacuum chamber formed by the diaphragm 44 due to flap seal 76 rising off port 78 on diaphragm top plate 80. With the vacuum released, as shown in FIGS. 7A to 7D, as the user is inhaling air through the inhaler 10, i.e. through the apertures 72 and all of the way along inside the cap housing 12 and main body 14 past the canister 50 and out through the central bore 68, the main compression spring 40 drives the lower cap 46, yoke 56 and canister 50 away from the cap housing 12 and towards the main body 14 and valve stem block 62 whereby the valve stem 54 is retracted into the canister 50. This places the pressurised metering chamber 82 in communication with valve stem block nozzle 64 so fires the canister and ejects inhalable substances from the metering chamber 82 through the nozzle 64 and mouthpiece 66 towards the lungs (not shown) of the user. The dose counter system 24 also registers a count by movement of the actuating pin 26 by the canister ferrule 220. At this time after opening and firing, the metering chamber 82 communicates with atmosphere. With the mouthpiece 66 left open such that the atmosphere communicates through the bore 88 and exit port 90 with the metering chamber 82, the metering chamber 82 can become at least partially or fully filled with gas such as air from the atmosphere.

In other embodiments comprising nasal inhalers, the mouthpiece 66 may be replaced with a nose piece.

As shown in FIGS. 8A to 8D, during closing, the mouthpiece dust cap 16 is rotated back to its closed position and the cams 60 push on the distal ends 59 of the drive rods 58 so as to push the yoke 56 towards the cap housing 12 so as to compress the main compression spring 40 again and the vacuum is formed again at the diaphragm 44. At the same time, the canister is pushed back to its original configuration of FIGS. 5A to 5D by the metering valve return spring 70.

As shown in FIG. 9, with the inhaler 10 in the configuration of FIGS. 5A to 5D, the metering valve spring 70 keeps the valve stem 54 extended, the inlet port 86 open and the exit port 90 effectively closed, i.e. with the metering chamber 82 isolated from atmosphere. At the same time the force F_{YL} applied as $F_{YL}/2$ by each of the legs or rods 58 of the yoke 56 to the lower cap 46 is greater than or equal to the force F_{FHUCS} applied in the opposite direction by the spring of the force holding unit 12.

As shown in FIG. 10, with the inhaler then changed to the configuration of FIGS. 6A to 6D, the canister is displaced to a representative distance D_{valve} from the canister position of FIG. 9 where this displacement at D_{valve} is less than the displacement required to actuate and fire a dose. In this FIG.

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10 configuration, the position of the canister 50 is determined by an equilibrium between forces, which is:

$$F_{\text{valve CS}} + F_{\text{Dia}} = F_{\text{FHU CS}}$$

where $F_{\text{valve CS}}$ is the force applied to the canister by the metering valve spring 70, F_{Dia} is the force applied by the partial vacuum in the diaphragm 44 in the same direction and $F_{\text{FHU CS}}$ is the opposing force applied by the compression spring 40 of the force holding unit 30. The port 78 is noted to be closed. The port 86 is open and the port 90 is closed.

As the user then inhales, the port 78 is opened by the action of air entering through the apertures 72 impinging on the flap 74, lifting flap seal 76. The equilibrium of FIG. 10 is therefore lost. The canister 50 is therefore moved to displace the valve stem 54 more, to the configuration of FIG. 11, so that the canister is a representative distance D_{Actuated} from the valve stem block 62, and where the force balance is that $F_{\text{valve CS}} \leq F_{\text{FHU CS}}$ in which the force applied to the lower cap 46 is less than or equal to the opposing force applied by the compression spring 40 of the force holding unit R. In this configuration, the port 86 has closed to isolate the metering chamber 82 from the interior reservoir 84 of the canister 50 and after this closure the port 90 has opened, thereby firing the canister 50 by venting pressurised contents within the metering chamber 82 out through the nozzle 64 of the valve stem block 62 for inhalation by the user.

The spring 40 is adapted such that the firing force $F_{\text{FHU CS}}$ is more than 35 N, typically less than 60 N. This may vary in other embodiments.

In most embodiments, the spring 40 is adapted in addition to device geometry such that the force exerted by the spring 40 on the valve/canister is equal to the sum of the opposing valve spring 70 and pneumatic resistance force in the FHU diaphragm 44 in the prepared position. Nonetheless, the spring 40, unless otherwise assisted, must be able to provide sufficient force once the mechanism is triggered to actuate the canister on inhalation. The specific force values will be dependent on the componentry of the device, driven predominantly by the force required to actuate the canister at a specific displacement, thus the spring 40 will be adapted to suit.

The metering valve 52 shown in FIG. 4 is similar to those described in U.S. Pat. No. 7,959,042B, which is incorporated by reference herein, and has the metering chamber 82 arranged for selective communication with either the interior reservoir 84 of the canister 50 via an inlet port 86, or with the interior bore 88 (FIGS. 5A to 5D) of the valve stem 54 which communicates via the valve stem block 62 with the nozzle 64, the valve stem 54 being provided with a radially configured capillary exit port 90 leading to the bore 88. The metering chamber 82 is at least partly defined by a cup-shaped inner metering body 92 and has an inner seal 94 and outer seal 96, as well as a location member 98, a main canister seal 100 and a crenelated valve stem driver 102 which has a through bore 104 axially directed towards the inlet port 86. The inlet port 86 includes two elongate openings 106 diametrically opposed to one another and which are defined by a pair of forked legs 108 which are spaced apart from one another by the elongated openings 106 and the open space forming the inlet port 86 between them. The forked legs 108 have substantially constant cross-section all the way along to their distal ends (not shown) which are located within the crenelated valve stem driver 102.

When the valve stem 54 is depressed into the canister 50 so that the inlet port 86 permits communication between the

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metering chamber 82 and the interior reservoir 84, the communication into the interior reservoir 84 is at an inner side 110 of the inner seal 94 and it will be appreciated that this is a slot-shaped porting between the forked legs 108 from where flow can travel directly axially into or out of the interior reservoir 84.

According to an alternative embodiment, the arrangement of openings in the metering valve of the present invention is similar to those described in US2016/0084385, which is incorporated by reference herein. In particular, the metering valve of the present invention may be similar to the embodiment shown in FIG. 4 of US2016/0084385, in which the valve body includes at least one first opening (i.e., at least one first side hole 100 that is arranged in a cylindrical portion of the valve body) and at least one second opening (i.e., at least one second side hole 111 that, as with the first hole(s), is arranged in a cylindrical portion of the valve body), the second opening(s) being axially offset relative to the first opening(s) along a longitudinal axis that extends between a first axial end and a second axial end of the valve body. The first opening(s) and second opening(s) that are axially offset from each other along the valve body enable the metering chamber to be filled and emptied.

The canister 50 includes inhalable substances including the active ingredient beclomethasone dipropionate and the propellant HFA134a which has a surface tension of about 8 mN/m as liquid at 25° C. Other active ingredients may be used in other embodiments, such as tiotropium bromide.

If the mouthpiece dust cap 16 is left open such that the atmosphere communicates through the bore 88 and exit port 90 with the metering chamber 82, the metering chamber can become at least partly or substantially fully filled with gas such as air from the atmosphere. When the mouthpiece dust cap 16 is closed, however, and when the interior reservoir 84 is oriented above the metering chamber 82, the present inventors have discovered that the liquid phase in the interior chamber can exchange places with gas in the metering chamber 82, the fluid travelling either directly through the openings 106 or through the throughbore 104, and along through the inner seal 94 and into the metering chamber 82 and gas in the metering chamber 82 can travel in the reverse direction along the same path, exiting with an axial component through between the forked legs 108 and through the elongated openings 106 into the interior reservoir 84. It is believed that the particular surface tension of the chosen propellant promotes this action and the higher density of the liquid than that of any gas in the metering chamber enabling the latter to rise up in and relative to the liquid.

The full filling of the metering chamber 82 with a dose of liquid from the interior reservoir 84 with any gas in the metering chamber passing in the reverse direction from the metering chamber 82 into the interior reservoir 84 is highly advantageous since with this one extension of the valve stem 54 from its retracted configuration after inhalation to its extended configuration with the mouthpiece dust cap 16 closed again ensures that the inhaler 10 is fully primed for use. This has overcome a significant problem.

As shown in FIG. 20, the inhaler 10 may be provided with a preventer 110 for preventing the user from taking a second or further inhalation while the dust cap 16 is still open. The preventer 110 may take the form of a warning signaller 102 such as a warning notice as shown in the drawing stating "to reload: close before each inhalation" although in other embodiments the preventer 110 could take various other forms such as an alarm or audible or visual warning device to indicate that the mouthpiece dust cap 16 is open and needs to be closed prior to the next inhalation.

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FIG. 21 is a graph showing a comparison of the inhaler of FIG. 1A with delivered dose for a prior art breath actuated inhaler with a different metering valve (not shown) in which the exit port from the interior reservoir comprises a radially oriented capillary bore which leads to an internal bore of the valve stem leading axially towards a further radially extending capillary port, such that the communication from the interior space is through the first capillary port, along the internal bore and out through the second radial capillary port into the metering chamber when the valve stem is in its extended configuration. In all cases the inhalers were held with the valve stems vertical and the canister interior reservoir above the metering chamber. After inhalation, the valve stem in each case was left in the retracted inhale configuration with the metering chamber exposed to atmosphere through the valve stem for the specified delay period and the inhaler was then reset and readied for inhalation, in the case of the present inhaler 10 by closing and opening the mouthpiece cap again. As shown by the graph of FIG. 21, with a target of 80 micrograms of BDP (beclomethasone dipropionate) the diamond shaped plots 205 are for the prior art inhaler which began to fail to reach 75% of the labelled claim for the dose after a delay of 30 seconds after inhalation in closing the mouthpiece cap to isolate the metering chamber from atmosphere. At all delays of 2 minutes or over, the prior inhaler failed to provide 75% of the labelled claim of dose in 100% of cases. This, the present inventors have discovered, is due to gas lock forming in the metering chamber after inhalation due to the metering chamber's exposure to atmosphere, i.e. in that when the mouthpiece cap is closed after a delay air is trapped in the metering chamber and is not replaced by liquid in the interior reservoir even when the metering chamber is connected to the interior reservoir. In contrast, the plots of crosses 207 in FIG. 21 show the performance of the inhaler of FIG. 1A. Here, 100% of the plots are in the range of 75 to 125% of labelled claim for the dose, even when there is no appreciable delay or a delay of one hour, twelve or twenty-four hours before closing the mouthpiece cap after inhalation. Therefore, even if the metering chamber 82 has been exposed to atmosphere for a relatively long time such that it is after that delay substantially full of gas due to evaporation/diffusion of substances after inhalation, this graph clearly shows that by closing the mouthpiece fully and opening it again, the gas in the metering chamber 82 is removed into the interior reservoir 84 and replaced with a correct dose very reliably.

Although FIG. 21 data is presented for 80 mcg (exactuator) targeted BDP HFA product, the data is representative of any formulation and formulation strength.

As shown in FIG. 12, the main body 14 has a tubular body portion 120 arranged to contain the pressurised canister 50 for sliding motion. As shown in FIG. 12, the valve stem block has a top surface 122 and the tubular body portion 120 has at least two mutually opposed guide ribs 124, 126. The guide ribs 124, 126 have substantially straight guide edges 130, 132 extending parallel to and spaced from one another, each straight guide edge 130, 132 having an upper corner 134, 136 where the straight guide edge meets a further surface 138, 140 of the ribs 124, 126 leading outwardly towards an upper rib section near an inner wall 146 of the tubular body portion 120. At least one of the ribs 124, 126 has its straight guide edge's upper corner 134, 136 positioned a distance D2 in a direction parallel to an axis of the valve stem block 62 along away from the top surface 122 of the valve stem block 62, a distance between the straight guide edges 130, 132 of the ribs 124, 126 perpendicular to the axis being ID2, and the ratio D2 divided by ID2 is 0.7.

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This is smaller than in previous embodiments and can surprisingly assist in providing smooth guiding of the canister within the tubular body portion 120.

The further surface 138, 140 of at least one of the guide ribs 124, 126 and in this case both of them extends away from the valve stem block 62 and terminates at a distance D3—in the case of guide rib 124—from the top surface 122 of the valve stem block 62 in the direction parallel to the axis, the ratio D3 divided by ID2 being 0.8, the equivalent ratio for the guide rib 126 being 1.0. Each guide rib meets the upper rib section 142, 144 near the inner wall 146 of the tubular body portion 120 at an outer rib position 148, 150 wherein the outer rib positions are a distance apart ID1 in a direction perpendicular to the axis 202 of the valve stem block 62 and the ratio ID2 divided by ID1 is 0.8. This arrangement assists beneficially in providing sufficient space for the canister 50 to move within the tubular body section 120.

With reference to FIG. 13, a portion of the main body 16 is shown with the mouthpiece dust cap 16 and the dose counter door 18 and the dose counter system 24 not yet installed. As can be seen, the dose counter chamber 22 includes a recess 152 for location of an end 154 (FIG. 3) of the return spring 28. The recess 152 has a substantially flat reaction surface for pushing on the end 154 of the return spring 28. The recess 152 also has a shoulder surface 158 adjacent the reaction surface 156 and an entrance mouth 160 into the reaction surface 156. A distinct guide surface 162, which is substantially planar is provided for guiding the end 154 of the return spring 28 into the recess 152 during assembly. The distinct guide surface 162 is wider than the entrance mouth 160 in a direction across the mouth and this assists substantially in assembling the spring 28 into the recess 152.

The entrance mouth 160 also has at least a chamfered entrance lip 164, an extension 166 of which into the guide surface forms a slanted edge 166 of the distinct guide surface 162. At least a portion of the distinct guide surface 162 comprises a portion of the body 14 which is recessed relative to the adjacent and partially surrounding portion 164 of the body by an edge 168. The edge 168 is particularly effective in catching the end 154 of the return spring and the wide guide surface 162 is effective in guiding the spring 28 past the chamfered entrance lip 164 and onto the reaction surface 156 where it remains once installed. A further edge 170 of the guide surface 162 is spaced from and generally parallel to the edge 168. The edge 170 forms an intersection with an adjacent portion 171 of the body 14.

As shown in FIG. 14A, the main body of the inhaler 10 includes a barrier 180 separating an interior space 182 defined at least partly by the tubular body portion 120 from the dose counter chamber 22. The barrier includes a stepped upper wall area 184 which has four steps 186, 188, 190, 192 at different levels. The steps are arcuate and have substantially flat parts 194, 196, 198, 200 aligned substantially perpendicular to the axis 202 of the valve stem block as well as a part-cylindrical risers 204, 206, 208 between the substantially flat parts 194, 196, 198, 200.

The arcuate steps 186, 188, 190, 192 are substantially concentric with the axis 202 of the valve stem block 62. The steps 186, 188, 190, 192 extend around the valve block 62 a distance/angle of about 170° although this is only approximate and may be in the region of about 180 to 120° in various embodiments. The material forming the barrier 180 is of substantially constant thickness throughout the steps 186, 188, 190, 192 which is advantageous for manufacturing techniques by moulding.

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As shown in FIG. 14B which is a view into the dose counter chamber 22, the dose counter chamber 22 is formed with two heat staking pins 212, 214 for attaching the dose counter system 24 permanently into position within the dose counter chamber 22. One of the heat staking pins 214 is directly attached to two of the steps 188, 190. The heat staking pin 214 is attached to one substantially flat step part 198 and to two step risers 206, 208, providing secure and advantageous location of the heat staking pin 214 in the stepped upper wall area 184 of the barrier 180. An aperture 218 for the actuating pin 26 of the dose counter system 24 is formed through the second furthest step part 198 away from the valve stem block 62.

The stepped upper wall area 184 is highly advantageous since it enables the accommodation of a length of movement of the canister 50 and in particular its ferrule 220 (FIG. 2) within the main body 14. Therefore, even with a metering valve 70 as used in the inhaler 10 which has a relatively long end-to-end travel of approximately 4 mm, the internal components can be maintained within a relatively small and compact inhaler 10, while also allowing for space in the dose counter chamber 22 for the dose counter system 24 and enabling the dose counter to be heat staked firmly in place by the heat stake pins 212, 214 including the pin 214 which is attached to the stepped upper wall area 84 of the barrier 180.

As shown in FIGS. 15A and 15B, the valve stem block 62 has the cylindrical inner bore 61 which has an inner diameter BD1 which has a first diameter, a seal 224 at an entrance to the inner bore 61 having a second diameter BD2 which is smaller than the first diameter. The seal 224 is inwardly convex and/or is toroidal. The first diameter BD1 is about 3.22 mm and is about 3.5% larger than the second diameter BD2. The valve system 54 has a cylindrical outer surface 226 (FIG. 2) with a diameter which is smaller than the first diameter BD1 but larger than the second diameter BD2 prior to introduction of the valve stem 54 into the inner bore 61 and is about 1% larger. The valve stem block 62 also includes an annular recess 228 which extends more than half way around the periphery of the inner bore 61, in this embodiment about 350° or more. The annular recess 228 has an inner diameter which is about 40% larger than the inner diameter BD1 of the cylindrical inner bore 61. This arrangement has been found to provide extremely effective sealing against blowback which has occurred in prior designs which have a substantially greater interference fit between the exterior diameter of the valve stem and the interior diameter of the inner bore of the valve stem. Surprisingly, and advantageously, using the inwardly convex seal 224 to the bore 61, very effective sealing without any blowback can be achieved even with a relatively small interference fit between the valve stem 54 and the seal 224, the annular recess 228 assisting in providing resilience to the valve stem block 62 for this purpose. The small interference fit allows for good sealing even when the inhaler 10 is subjected to high temperatures for long periods since there is little stress to relieve. Furthermore, the seal 224 permits a relatively low insertion force for inserting the valve stem 54 into the valve stem block 62 and this enables accurate positioning of these two components relative to one another in an axial direction of the valve stem 54 so that the dose counter system 24 can count reliably by way of accurate actuation of its actuator pin 26 by the canister ferrule 220.

As shown in the various sectional views of FIGS. 16A through to 18C, a lock system 250 is provided for locking the cap housing or force holding unit housing 12 on the main body 14. Helical threads 252, 254 are provided, with male

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threads 252 on the cap housing 12 and female threads 254 on the main body 14, for rotational attachment of the cap housing 12 on the main body 14 and for resisting relative longitudinal movement therebetween without rotation.

The lock system 250 includes a protrusion 256 in the region of the helical thread 254 on the main body 14 which is lockable in a recess 258 in the region of the helical thread 252 on the cap housing. As shown in FIG. 17C, the inhaler 10 includes two of the protrusions 256 in two of the recesses 258 formed at opposing locations on the inhaler, i.e. diametrically opposite to one another. As shown in FIG. 18A, each protrusion 256 has a leading ramp surface 260 and a trailing ramp surface 266, the included angle A between the ramp and trailing surfaces 260, 266 being 115°, although a range of about 95 to 120° is envisaged. The recesses have a similar included angle which is smaller than the angle of the protrusion 256 at about 100°. This ensures that the protrusion 256 will fit securely in the recess 258 without any play rotationally.

The main body 14 has a central axis 202 coincident with that 202 of the valve stem block 62 and the ramp surfaces 266 are inclined at an angle of about 45°±15° to tangential.

The lock system 250 also includes a first lock member 270 on the cap housing 12 which is adapted to engage a second lock member 272 at a lock interface 274 formed by respective engagement faces thereof, the lock interface 274 being oriented substantially perpendicular to tangential. This therefore assists in preventing rotation. The first lock member 270 has a radial extent of 0.39 mm, although about 0.35 to 0.45 mm is envisaged in other embodiments or 0.25 to 0.75 mm. The second lock member 272, it will be appreciated, has a greater radial extent. The first lock member 270 has a longitudinal extent parallel to the axis 202 of about 10 mm.

The main body 14 and cap housing 12 are formed of plastics material and the lock system 250 is configured so that a release torque required to overcome the locking provided by the plastics main body and cap housing at the lock interface 274 and at the protrusions 256 and recesses 258 is more than 1 Nm. In the described example, the release torque is about 2.75 Nm. When an information sticker is applied over the top of the interface between the main body 14 and cap housing 12 the release torque may rise to about 3.5 Nm. This has been found to be lower than 4 Nm and this is low enough that a laboratory is capable of opening up the inhaler 10 for inspection without significant destruction. However, this level of torque is significantly higher than likely to be tried by a user in an attempt to open the inhaler 10 which might result in tampering and damage to the components of the inhaler 10.

In an alternative design, the radial extent of the first locking member 270 is significantly greater at about 0.73 mm and this has been found, surprisingly, to provide a removal torque which is considered too high at 4.6 Nm for laboratory disassembly without destruction. In contrast, a design omitting the first lock member 270 was found to provide a removal torque of only 0.7 Nm which is considerably too low and likely to result in users rotating the cap housing 12 off the main body 14 and potentially damaging the inhaler by investigating the contents. In fact, this was the first design attempted by the present inventors and the next step was to double up the number of protrusions 256 and recesses 258 so that there are four in total in an attempt to double the torque, at least, from 0.7 Nm. However, surprisingly, with this design, the removal torque was only increased by about 10% to 0.8 Nm. The ideal remove torque was surprisingly achieved with only one protrusion 256 on

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each thread **254** and with a locking member **270** with only a small radial extent of 0.39 mm. The locking member **270** advantageously also includes a lead ramp **290** for achieving a smooth snap lock of the cap housing **12** onto the main body **14** when the cap housing **12** is twisted into the locked position.

FIG. **19** shows a modification of the inhaler **10** to form an inhaler **1000** which is a metered dose inhaler having a main body **1002** and mouthpiece dust cap **1004** for the mouthpiece **1006** for stopping foreign objects entering the central bore **1008** of the mouthpiece **1006** and for protecting the mouthpiece generally. This metered dose inhaler **1000** does not include the cap housing **12** or the force holding unit **30** or yoke **56** but it does include the same dose counter chamber **22**, dose counter system **24**, canister **50** and metering valve **52** and valve stem **54** and valve stem block **62** as that in the inhaler **10**. If this metered dose inhaler is left with the canister **50** accidentally depressed, for example while squashed in luggage or clothing by mistake, such that the metering chamber is left exposed to the atmosphere for a considerable period of time, then when the inhaler **1000** is located and turned upright for use with respective gravity with the canister allowed to extend to its rest position in which the metering chamber communicates with the interior reservoir, any gas such as air which has entered the metering chamber is easily expelled up into the interior reservoir of the canister just as in the inhaler **10** such that an accurate next dose is applied and the problem of gas lock is therefore avoided.

Inhalers in accordance with preferred embodiments of the present invention are suitable for the delivery of many classes of active ingredients by inhalation, and may be used for the treatment of various diseases and disorders. According to preferred embodiments, the inhaler is used for the treatment of respiratory disorders (e.g., COPD, asthma and/or cystic fibrosis). The inhaler may also be used to treat non-respiratory disorders, such as migraine. According to an embodiment, a method of treating a respiratory disease or disorder comprises actuating the inhaler to administer a therapeutically effective amount of one or more active ingredients. As described herein, the canister of the inhaler contains a drug formulation comprising one or more active ingredients in suspension or in solution. Preferably, the drug formulation comprises one or more active ingredients in propellant (e.g., HFA). The drug formulation may optionally comprise one or more excipients in combination with the active ingredient(s) and propellant.

In certain embodiments, the inhaler described herein can be used to treat patients suffering from a disease or disorder selected from asthma, chronic obstructive pulmonary disease (COPD), exacerbation of airways hyper reactivity consequent to other drug therapy, allergic rhinitis, sinusitis, pulmonary vasoconstriction, inflammation, allergies, impeded respiration, respiratory distress syndrome, pulmonary hypertension, pulmonary vasoconstriction, and any other respiratory disease, condition, trait, genotype or phenotype that can respond to the administration of, for example, a long-acting muscarinic antagonist (LAMA), long-acting β 2-adrenergic agonist (LABA), corticosteroid, or other active agent as described herein, whether alone or in combination with other therapies. In certain embodiments, the compositions, systems and methods described herein can be used to treat pulmonary inflammation and obstruction associated with cystic fibrosis. As used herein, the terms "COPD" and "chronic obstructive pulmonary disease" may encompass chronic obstructive lung disease (COLD), chronic obstructive airway disease (COAD), chronic airflow

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limitation (CAL) and chronic obstructive respiratory disease (CORD) and include chronic bronchitis, bronchiectasis, and emphysema. As used herein, the term "asthma" refers to asthma of whatever type or genesis, including intrinsic (non-allergic) asthma and extrinsic (allergic) asthma, mild asthma, moderate asthma, severe asthma, bronchitic asthma, exercise-induced asthma, occupational asthma and asthma induced following bacterial infection. Asthma is also to be understood as embracing wheezy-infant syndrome.

A range of classes of active ingredients have been developed to treat respiratory disorders and each class has differing targets and effects.

Bronchodilators are employed to dilate the bronchi and bronchioles, decreasing resistance in the airways, thereby increasing the airflow to the lungs. Bronchodilators may be short-acting or long-acting. Typically, short-acting bronchodilators provide a rapid relief from acute bronchoconstriction, whereas long-acting bronchodilators help control and prevent longer-term symptoms.

Different classes of bronchodilators target different receptors in the airways. Two commonly used classes are anticholinergics and β 2-agonists.

Anticholinergics (or "antimuscarinics") block the neurotransmitter acetylcholine by selectively blocking its receptor in nerve cells. On topical application, anticholinergics act predominantly on the M3 muscarinic receptors located in the airways to produce smooth muscle relaxation, thus producing a bronchodilatory effect. Non-limiting examples of long-acting muscarinic antagonists (LAMA's) include tiotropium (bromide), oxitropium (bromide), aclidinium (bromide), ipratropium (bromide) glycopyrronium (bromide), oxybutynin (hydrochloride or hydrobromide), tolterodine (tartrate), trospium (chloride), solifenacin (succinate), fesoterodine (fumarate), darifenacin (hydrobromide) and umeclidinium (bromide). In each case, particularly preferred salt/ester forms are indicated in parentheses.

β 2-Adrenergic agonists (or " β 2-agonists") act upon the β 2-adrenoceptors and induce smooth muscle relaxation, resulting in dilation of the bronchial passages. Non-limiting examples of long-acting β 2-adrenergic agonists (LABA's) include formoterol (fumarate), salmeterol (xinafoate), indacaterol (maleate), bambuterol (hydrochloride), clenbuterol (hydrochloride), olodaterol (hydrochloride), carmoterol (hydrochloride), tulobuterol (hydrochloride) and vilanterol (triphenylacetate). Non-limiting examples of short-acting β 2-agonists (SABA's) include albuterol (sulfate) and levalbuterol (tartrate). In each case, particularly preferred salt/ester forms are indicated in parentheses.

According to one embodiment, the formulation comprises albuterol (sulfate).

Another class of active ingredients employed in the treatment of respiratory disorders are inhaled corticosteroids (ICS's). ICS's are steroid hormones used in the long-term control of respiratory disorders. They function by reducing the airway inflammation. Non-limiting examples of inhaled corticosteroids include budesonide, beclomethasone (dipropionate), fluticasone (propionate), mometasone (furoate), ciclesonide and dexamethasone (sodium).

According to one embodiment, the formulation comprises beclomethasone dipropionate.

According to an embodiment, the inhaler delivers one or more active ingredients selected from the group consisting of tiotropium (bromide), oxitropium (bromide), aclidinium (bromide), ipratropium (bromide) glycopyrronium (bromide), oxybutynin (hydrochloride or hydrobromide), tolterodine (tartrate), trospium (chloride), solifenacin (succinate), fesoterodine (fumarate), darifenacin (hydrobromide),

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umeclidinium (bromide), formoterol (fumarate), salmeterol (xinafoate), indacaterol (maleate), bambuterol (hydrochloride), clenbuterol (hydrochloride), olodaterol (hydrochloride), carmoterol (hydrochloride), tulobuterol (hydrochloride), vilanterol (triphenylacetate), albuterol (sulfate), 5 levalbuterol (tartrate), budesonide, beclomethasone (dipropionate), fluticasone (propionate), mometasone (furoate), ciclesonide, dexamethasone (sodium) and a combination thereof.

According to particular embodiments, the inhaler delivers a combination of at least two different active ingredients (two, three, four, etc.) which belong to the same or different classes. According to one embodiment, the inhaler delivers a “triple combination” of three different active ingredients. The three active ingredients may belong to three different active ingredient classes (e.g., LAMA, LABA, ICS); alternatively, two or three of the active ingredients may belong to the same class.

According to additional embodiments, the inhaler delivers one or more active ingredients selected from the group consisting of a long-acting muscarinic antagonist (LAMA), a long-acting β 2-adrenergic agonist (LABA), an inhaled corticosteroid (ICS) and a combination thereof. Thus, the inhaler may deliver a formulation comprising one or more LAMA's, one or more LABA's and one or more ICS's. That is, the device may deliver a double combination of a LAMA and a LABA, a LAMA and an ICS, or a LABA and an ICS; or a triple combination of a LAMA, a LABA and an ICS.

According to an alternative embodiment, the inhaler delivers one or more active ingredients for the treatment of a headache disorder, such as migraine. For example, the inhaler may deliver dihydroergotamine (DHE) or a pharmaceutically acceptable salt thereof, such as dihydroergotamine mesylate.

In one embodiment the inhaler comprises a reservoir, particularly a pressurized canister, comprising an active ingredient.

Preferably the active ingredient is presented in a pharmaceutical formulation comprising a propellant, optionally a co-solvent and optionally other pharmaceutically acceptable excipients.

Preferred propellants include hydrofluoroalkanes, in particular 1,1,1,2-tetrafluoroethane (HFA134a), 1,1,1,2,3,3,3-heptafluoropropane (HFA227), or combinations thereof. Most particular propellant is HFA134a. Most particular HFA134a concentration is from about 91.8% w/w to 92.9% w/w.

HFA134a has a low boiling point (-26.1°C .) and correspondingly high vapor pressure (572 kpa) at 20°C .

Particular co-solvents are selected from the list of aliphatic alcohols (particularly ethanol), glycerols and glycols. Most particular co-solvent is ethanol. Most particular ethanol concentration is about 8% w/w.

Ethanol is well known to be compatible with HFA-134a and increases the solubility of BDP. Ethanol (anhydrous) is used as a co-solvent to aid solubility of BDP in HFA134a. A concentration of around 8% w/w of ethanol is known to provide necessary stability, preventing precipitation and achieving correct aerosol performance.

Other pharmaceutically acceptable excipients include surfactants, particularly oleic acid. Preferably, the active ingredient is suspended in the propellant. Alternatively the active ingredient is dissolved in the propellant. The active ingredient may also be partly suspended and partly dissolved in the propellant.

A particular active ingredient is selected from the group consisting of anti-inflammatory agents, β 2-adrenoreceptor

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agonists, anti-cholinergic agents, anti-histamines, serotonin agonists, and combinations thereof.

A particular corticosteroid is beclomethasone dipropionate (BDP).

A particular β 2-adrenoreceptor agonist is salbutamol sulphate.

In a particular embodiment of the invention, the active ingredient is selected from beclomethasone dipropionate (BDP), salbutamol sulphate and dihydroergotamine.

In a particular embodiment the inhaler comprises a pressurized canister comprising beclomethasone dipropionate as active ingredient, HFA134a as propellant and ethanol as co-solvent.

In a particular embodiment the inhaler comprises a pressurized canister comprising beclomethasone dipropionate as active ingredient at about 1.0 mg/ml, HFA134a as propellant at about 1090.20 mg/ml and ethanol as co-solvent at about 94.80 mg/ml.

In a particular embodiment the inhaler comprises a pressurized canister comprising beclomethasone dipropionate as active ingredient at about 0.084% w/w, HFA134a as propellant at about 91.9% w/w and ethanol as co-solvent at about 8.0% w/w.

In a particular embodiment the inhaler comprises a pressurized canister comprising beclomethasone dipropionate as active ingredient at about 0.169% w/w, HFA134a as propellant at about 91.8% w/w and ethanol as co-solvent at about 8.0% w/w.

In a particular embodiment the inhaler comprises a pressurized canister comprising salbutamol sulphate as active ingredient, HFA134a as propellant and ethanol as co-solvent.

In a particular embodiment the inhaler comprises a pressurized canister comprising about 0.1098 mg of salbutamol sulphate as active ingredient, about 27.8 mg of HFA134a as propellant and about 3.6 mg of ethanol as co-solvent.

One embodiment relates to an inhaler as described herein comprising an active ingredient.

One embodiment relates to an inhaler as described herein comprising an active ingredient for therapeutic use.

One embodiment relates to an inhaler as described herein comprising an active ingredient for use in the treatment or prevention of a respiratory disease, particularly COPD or Asthma.

One embodiment relates to an active ingredient for use in the treatment or prevention of a respiratory disease, particularly COPD or Asthma, wherein the active ingredient is delivered to a patient using an inhaler as described herein.

One embodiment relates to a method for the treatment or prevention of respiratory diseases, particularly COPD or Asthma, which method comprises administering an active ingredient to a human being or animal using an inhaler as described herein.

One embodiment relates to the use of an inhaler as described herein comprising an active ingredient for the treatment or prevention of respiratory diseases, particularly COPD or Asthma.

Embodiments of the present invention may be further understood by reference to the Example provided below.

EXAMPLE

According to the following example, a method of using the inhaler of the present invention comprises delivering a therapeutically effective amount of beclomethasone dipropionate HFA for the treatment of asthma, particularly for the maintenance treatment of asthma as prophylactic therapy in

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patients 4 years of age and older, wherein the inhaler is a breath-actuated inhaler (BAI) as described herein and the step of actuating the inhaler comprises inhaling through the inhaler. The breath-actuated inhaler may be used by patients to deliver at least about 40 mcg beclomethasone dipropionate upon each actuation, preferably twice daily, e.g., it may be used by patients 4 to 11 years old to deliver 40 mcg or 80 mcg beclomethasone dipropionate twice daily, or may be used by patients 12 years of age and older to deliver 40 mcg, 80 mcg, 160 mcg or 320 mcg beclomethasone dipropionate twice daily. Actuation of the breath-actuated inhaler is preferably triggered by an inspiratory flow rate of at least about 20 liters per minute (L/min), and includes a primeless valve so that no priming actuations are required before use. A method of treating asthma may comprise inhaling through the BAI at a flow rate of at least about 20 L/min without priming the inhaler before use, wherein the inhaler comprises a primeless valve as described herein and wherein the mean change from baseline for FEV₁ between 2-6 weeks or between 2-12 weeks or between 4-12 weeks of using the BAI is greater than about 0.150 L or greater than about 0.200 L. Preferably, the mean peak plasma concentration (C_{max}) of BDP is between about 6000 pg/mL and about 7000 pg/mL or between about 6200 pg/mL and about 6800 pg/mL at 2 minutes after inhalation of 320 mcg using the BAI (4 inhalations of the 80 mcg/inhalation strength). The mean peak plasma concentration of the metabolite 17-BMP is preferably between about 1000 pg/mL and about 2000 pg/mL or between about 1200 pg/mL and about 1700 pg/mL at 10 minutes after inhalation of 320 mcg of the BAI.

The breath-actuated inhaler (BAI) in this example included a canister having an interior reservoir containing pressurised inhalable substances including fluid; a "primeless" metering valve including a metering chamber and a valve stem defining a communication path between the metering chamber and the interior reservoir, the communication path including an opening configured to permit flow between a transfer space inside the valve stem and the interior reservoir, the interior reservoir being arranged for orientation above the metering chamber whereby gas such as air located within the metering chamber is replaced with liquid from the interior reservoir. Preferably, the primeless metering valve is the embodiment shown in FIG. 4 and described in U.S. Pat. No. 7,959,042B. Alternatively, the primeless metering valve is similar to the embodiment shown in FIG. 4 of US2016/0084385, as described herein.

Two confirmatory Phase 3 clinical trials were conducted comparing the above-described breath-actuated inhaler with placebo in adult and adolescent patients with persistent asthma (Trial 1 and Trial 2).

Trial 1: This randomized, double-blind, parallel-group, placebo-controlled, 12-week, efficacy and safety trial compared the breath-actuated inhaler 40 and 80 mcg given as 1 inhalation twice daily with placebo in adult and adolescent patients with persistent symptomatic asthma despite low-dose inhaled corticosteroid or non-corticosteroid asthma therapy. Patients aged 12 years and older who met the entry criteria including FEV₁ 40-85 percent of predicted normal, reversible bronchoconstriction of 15% with short-acting inhaled beta-agonist entered a 14-21 day run-in period. 270 patients (104 previously treated with inhaled corticosteroids) who met all the randomization criteria including asthma symptoms and rescue medication use were discontinued from asthma maintenance medication and randomized equally to treatment with the breath-actuated inhaler (BAI) 80 mcg/day BDP, the breath-actuated inhaler 160 mcg/day BDP or placebo. Baseline FEV₁ values were simi-

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lar across treatments. The primary endpoint for this trial was the standardized baseline-adjusted trough morning forced expiratory volume in 1 second (FEV₁) area under the effect curve from time zero to 12 weeks [FEV₁ AUEC(0-12 wk)]. Patients in both treatment groups had significantly greater improvements in trough FEV₁ compared to placebo (BAI 80 mcg/day, LS mean change of 0.124 L and BAI 160 mcg/day, LS mean change of 0.116 L over 12 weeks). In addition, the mean change from baseline for FEV₁ was greater than about 0.150 L between week 4 through week 12 (generally between about 0.150 L and about 0.250 L). Both doses of BAI were effective in improving asthma control with significantly greater improvements in FEV₁ and morning PEF when compared to placebo. Reduction in asthma symptoms was also supportive of the efficacy of the BAI.

Trial 2: This randomized, double-blind, parallel-group, placebo-controlled, 6-week, efficacy and safety trial compared BAI 40 and 80 mcg BDP given as 4 inhalations twice daily and placebo in adult and adolescent patients with persistent symptomatic asthma despite treatment with non-corticosteroid, inhaled corticosteroids (with or without a long acting beta agonist [LABA]), or combination asthma therapy. The study also included a reference treatment group, QVAR® Inhalation Aerosol (QVAR MDI) 40 mcg, 4 inhalations twice daily. Patients aged 12 years and older who met the entry criteria including FEV₁ 50-90% predicted normal, reversible bronchoconstriction of at least 10% with short-acting inhaled beta-agonist discontinued baseline asthma treatment and entered a 2-4 week run-in period. 425 patients (257 previously treated with ICS with or without LABA) who met all the randomization criteria including FEV₁ of 40-85% predicted and 15% reversibility with short-acting inhaled beta-agonist, and asthma symptoms were randomized equally to the BAI 320 mcg/day, BAI 640 mcg/day, QVAR MDI 320 mcg/day or placebo. Baseline FEV₁ values were similar across treatments. The primary endpoint for this trial was the standardized baseline-adjusted trough morning forced expiratory volume in 1 second (FEV₁) area under the effect curve from time zero to 6 weeks [FEV₁ AUEC(0-6 wk)]. Patients in both treatment groups had significantly greater improvements in trough FEV₁ compared to placebo (BAI 320 mcg/day, LS mean change of 0.144 L and BAI 640 mcg/day, LS mean change of 0.150 L over 12 weeks). Treatment with QVAR MDI was similar. The change from baseline in morning FEV₁ during the trial was greater than 0.150 L or 0.200 L between week 2 through week 6 (generally between about 0.150 L and about 0.250 L). Both doses of the BAI were effective in improving asthma control with significantly greater improvements in FEV₁, morning PEF, weekly average of daily trough morning FEV₁, reduced rescue medication use and improved asthma symptom scores than with placebo. Similar results were demonstrated with QVAR MDI.

The inhaler of the present disclosure has broad application. The apparatuses and associated methods in accordance with the present disclosure have been described with reference to particular embodiments thereof in order to illustrate the principles of operation. The above description is thus by way of illustration and not by way of relative and directional references (including: upper, lower, upward, downward, left, right, leftward, rightward, top, bottom, side, above, below, front, middle, back, vertical, horizontal, height, depth, width, and so forth) are normally given by way of example to aid the reader's understanding of the particular embodiments described herein. They should not be read to be requirements or limitations, particularly as to the position, orientation, or use of the invention unless specifically set

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forth in the claims. Connection references (e.g., attached, coupled, connected, joined, secured and the like) are to be construed broadly and may include intermediate members between a connection of elements and relative movement between elements. As such, connection references do not necessarily infer that two elements are directly connected and in fixed relation to each other, unless specifically set forth in the claims.

Various modifications may be made to the embodiments described without departing from the scope of the invention as defined by the accompanying claims.

What is claimed is:

1. A breath actuated inhaler having a drive adapted to drive a pressurized canister so as to retract a metering valve stem into the pressurized canister to fire the pressurized canister, the pressurized canister comprising a metering chamber and an interior reservoir, and being adapted to move during operation between 1 and 4 mm between end positions of its length of travel relative to the valve stem, the drive being arranged to apply a firing force of greater than 35 N and less than 60 N to the pressurized canister at a position of the pressurized canister relative to the valve stem at which the pressurized canister fires, the breath actuated inhaler further having a metering valve spring and a dose counter with a dose counter biasing element that cooperate together with the drive to hold the pressurized canister in a ready-to-fire configuration in which the pressurized canister is displaced from the end positions and the metering chamber is isolated from the atmosphere and wherefrom, in response to air flow, the pressurized canister is movable to close communication between the metering chamber and the interior reservoir and to open communication between the metering chamber and the atmosphere, and a vacuum chamber external to the metering chamber, wherein the metering valve spring and the dose counter biasing element combine with a vacuum force from the vacuum chamber to oppose a force from the drive when the pressurized canister is in the ready-to-fire configuration.

2. The breath actuated inhaler of claim 1 in which the drive comprises a drive spring.

3. The breath actuated inhaler of claim 1 in which the pressurized canister is arranged to move between 1 and 3 mm between the end positions.

4. The breath actuated inhaler of claim 1 in which the drive is adapted to provide the firing force as more than 40 N and less than 60 N.

5. The breath actuated inhaler of claim 1 in which the firing force is more than equal to that required to fire the pressurized canister.

6. The breath actuated inhaler of claim 1 wherein the dose counter biasing element comprises a dose counter return spring, and wherein the firing force is greater than the sum at the point of firing of opposing forces applied to the pressurized canister by the metering valve spring in the pressurized canister and the dose counter return spring.

7. The breath actuated inhaler of claim 1 wherein the interior reservoir contains a hydrofluoroalkane propellant.

8. The breath actuated inhaler of claim 7 wherein the propellant comprises a cosolvent.

9. The breath actuated inhaler of claim 1 wherein the interior reservoir contains one or more active ingredients.

10. The breath actuated inhaler of claim 9, wherein the one or more active ingredients comprise beclomethasone dipropionate or tiotropium bromide.

11. The breath actuated inhaler of claim 1 wherein the pressurized canister comprises a primeless metering valve.

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12. The breath actuated inhaler of claim 1 further comprising an actuator system for operating the drive.

13. The breath actuated inhaler of claim 12 wherein the actuator system including the vacuum chamber external to the metering chamber has a vacuum release system operable to permit the drive to drive movement of the pressurized canister relative to the valve stem.

14. The breath actuated inhaler of claim 13 wherein the vacuum release system is air flow actuable.

15. The breath actuated inhaler of claim 12 wherein the actuator system or drive includes or is operated as a latch, trigger or switch.

16. The breath actuated inhaler of claim 1 wherein the drive is configured to hold the valve stem depressed with the metering chamber of the pressurized canister communicating with atmosphere.

17. A method of treating a respiratory disease or disorder comprising actuating the inhaler of claim 1 to administer a therapeutically effective amount of one or more active ingredients.

18. The method of claim 17, wherein the step of actuating the inhaler comprises inhaling through the inhaler.

19. The method of claim 17, wherein the respiratory disease or disorder is asthma.

20. The method of claim 17, wherein the respiratory disease or disorder is COPD.

21. The method of claim 17, wherein the one or more active ingredients comprise a corticosteroid.

22. The method of claim 17, wherein the one or more active ingredients comprise beclomethasone dipropionate or tiotropium bromide.

23. The method of claim 17, wherein the pressurized canister is adapted to move during operation about 4 mm between end positions of its length of travel relative to the valve stem.

24. The breath actuated inhaler of claim 1, wherein the dose counter biasing element comprises a dose counter return spring.

25. A breath actuated inhaler having a drive adapted to drive a pressurized canister so as to retract a metering valve stem into the pressurized canister to fire the pressurized canister, the pressurized canister comprising a metering chamber and an interior reservoir, and being adapted to move during operation between 1 and 4 mm between end positions of its length of travel relative to the valve stem, the drive being arranged to apply a firing force of greater than 35 N and less than 60 N to the pressurized canister at a position of the pressurized canister relative to the valve stem at which the pressurized canister fires, the breath actuated inhaler further having a metering valve spring and a dose counter with a dose counter biasing element that cooperate together with the drive to hold the pressurized canister in a ready-to-fire configuration in which the pressurized canister is displaced from the end positions and the metering chamber is isolated from the atmosphere and wherefrom, in response to air flow, the pressurized canister is movable to close communication between the metering chamber and the interior reservoir and to open communication between the metering chamber and the atmosphere, the breath actuated inhaler further having an actuator system for operating the drive, wherein the actuator system includes a vacuum chamber external to the metering chamber having a vacuum release system operable to permit the drive to drive movement of the pressurized canister relative to the valve stem, and the metering valve spring, a vacuum force from the vacuum chamber, and the dose counter biasing element

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combine to oppose a force from the drive when the pressurized canister is in the ready-to-fire configuration.

26. The breath actuated inhaler of claim 25 wherein the vacuum release system is air flow actuatable.

27. The breath actuated inhaler of claim 25 wherein the actuator system or drive includes or is operated as a latch, trigger or switch.

28. The breath actuated inhaler of claim 25 wherein the dose counter biasing element comprises a dose counter return spring, and wherein the firing force is greater than the sum at the point of firing of opposing forces applied to the pressurized canister by the metering valve spring in the pressurized canister and the dose counter return spring.

29. The breath actuated inhaler of claim 25 wherein the drive is configured to hold the valve stem depressed with the metering chamber of the pressurized canister communicating with atmosphere.

30. A method of treating a respiratory disease or disorder comprising actuating the inhaler of claim 25 to administer a therapeutically effective amount of one or more active ingredients.

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EXHIBIT J

(12) **United States Patent**
Walsh et al.(10) **Patent No.:** **US 11,395,889 B2**(45) **Date of Patent:** **Jul. 26, 2022**(54) **DOSE COUNTER FOR INHALER HAVING AN ANTI-REVERSE ROTATION ACTUATOR**(71) Applicants: **Ivax Pharmaceuticals Ireland**,
Waterford (IE); **Norton (Waterford) Limited**, Waterford (IE); **Teva Pharmaceuticals Ireland**, Waterford (IE)(72) Inventors: **Declan Walsh**, County Kilkenny (IE); **Derek Fenlon**, County Wexford (IE); **Simon Kaar**, County Cork (IE); **Jan Geert Hazenberg**, County Kilkenny (IE); **Daniel Buck**, County Waterford (IE); **Paul Clancy**, Waterford (IE); **Robert Charles Uschold**, Leominster, MA (US); **Jeffrey A. Karg**, Hopkinton, MA (US)(73) Assignees: **Ivax Pharmaceuticals Ireland**,
Waterford (IE); **Norton (Waterford) Limited**, Waterford (IE); **Teva Pharmaceuticals Ireland**, Waterford (IE)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: **16/915,558**(22) Filed: **Jun. 29, 2020**(65) **Prior Publication Data**

US 2021/0016026 A1 Jan. 21, 2021

Related U.S. Application Data

(60) Continuation of application No. 15/804,735, filed on Nov. 6, 2017, now Pat. No. 10,695,512, which is a continuation of application No. 15/269,249, filed on Sep. 19, 2016, now Pat. No. 9,808,587, which is a continuation of application No. 14/103,324, filed on Dec. 11, 2013, now Pat. No. 9,463,289, which is a division of application No. 13/110,532, filed on May 18, 2011, now Pat. No. 8,978,966.

(Continued)

(51) **Int. Cl.****A61M 15/00** (2006.01)**G06M 1/24** (2006.01)**A61M 11/00** (2006.01)(52) **U.S. Cl.**CPC **A61M 15/0078** (2014.02); **A61M 11/00** (2013.01); **A61M 15/007** (2014.02);
(Continued)(58) **Field of Classification Search**CPC A61M 15/0078; A61M 15/0025; A61M 15/0026; A61M 15/007; A61M 15/0071;
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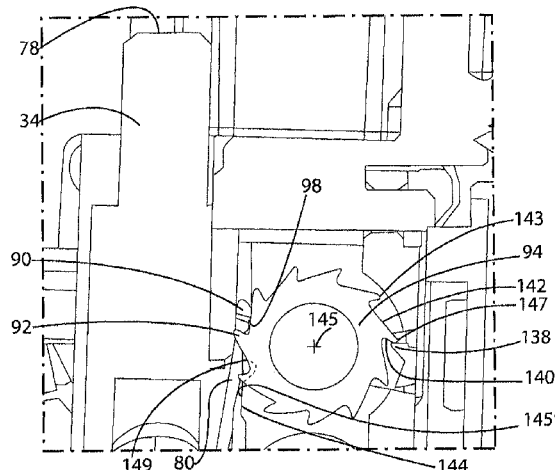
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(Continued)*Primary Examiner* — Daniel A Hess(74) *Attorney, Agent, or Firm* — Morgan, Lewis & Bockius LLP(57) **ABSTRACT**

An inhaler includes a main body having a canister housing, a medicament canister retained in a central outlet port of the canister housing, and a dose counter having an actuation member for operation by movement of the medicament canister. The canister housing has an inner wall, and a first inner wall canister support formation extending inwardly from a main surface of the inner wall. The canister housing

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has a longitudinal axis X which passes through the center of the central outlet port. The first inner wall canister support formation, the actuation member, and the central outlet port lie in a common plane coincident with the longitudinal axis X such that the first inner wall canister support formation protects against unwanted actuation of the dose counter by reducing rocking of the medicament canister relative to the main body of the inhaler.

6 Claims, 17 Drawing Sheets

Related U.S. Application Data

- (60) Provisional application No. 61/417,659, filed on Nov. 29, 2010, provisional application No. 61/345,763, filed on May 18, 2010.

(52) U.S. Cl.

CPC *A61M 15/009* (2013.01); *A61M 15/0025* (2014.02); *A61M 15/0026* (2014.02); *A61M 15/0065* (2013.01); *A61M 15/0071* (2014.02); *G06M 1/246* (2013.01); *A61M 2202/064* (2013.01); *A61M 2205/6063* (2013.01); *A61M 2207/00* (2013.01); *A61M 2207/10* (2013.01); *Y10T 29/49* (2015.01); *Y10T 29/49764* (2015.01); *Y10T 29/49826* (2015.01)

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CPC A61M 11/00; A61M 15/0065; A61M 15/009; G06M 1/246
USPC 128/203.12
See application file for complete search history.

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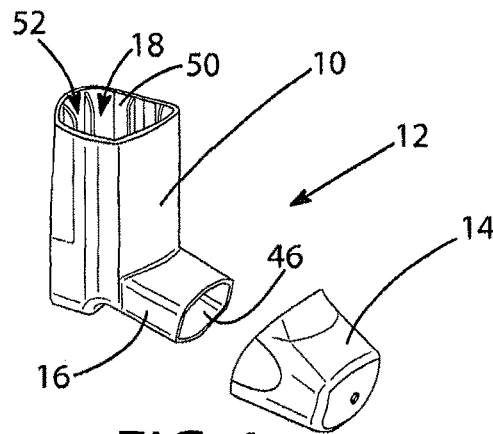


FIG. 1

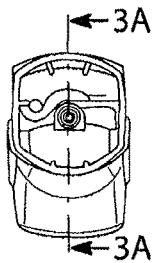


FIG. 2

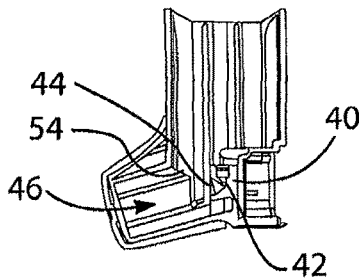


FIG. 3A

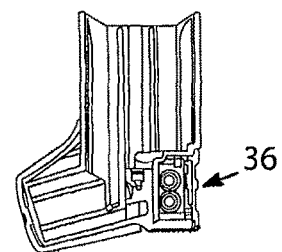


FIG. 3B

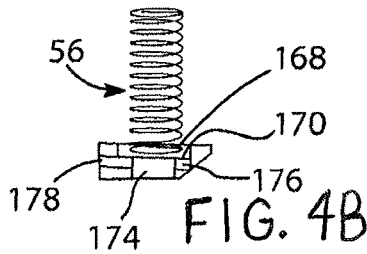


FIG. 4B

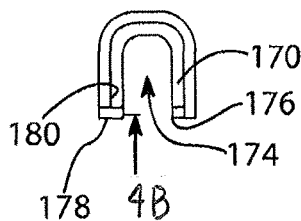


FIG. 4C

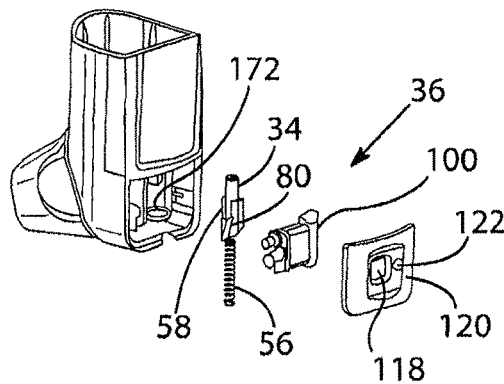


FIG. 4A

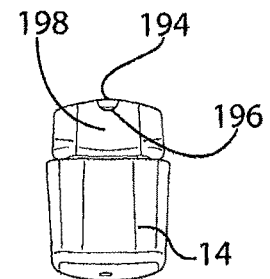


FIG. 5

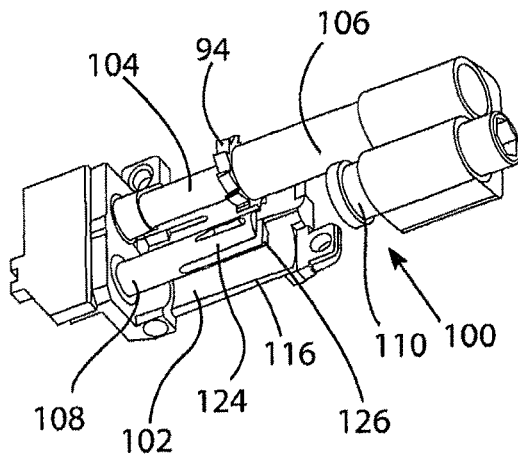


FIG. 6A

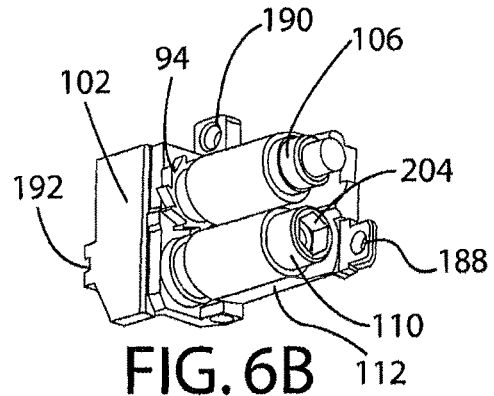


FIG. 6B

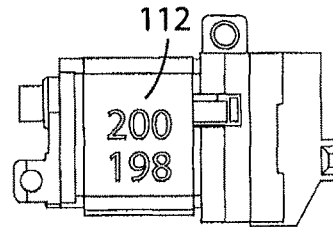


FIG. 6C

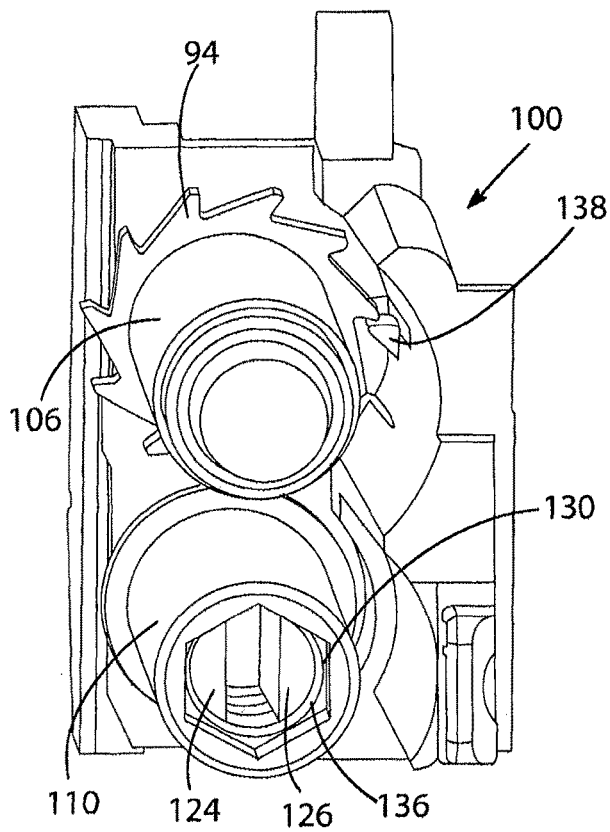


FIG. 6D

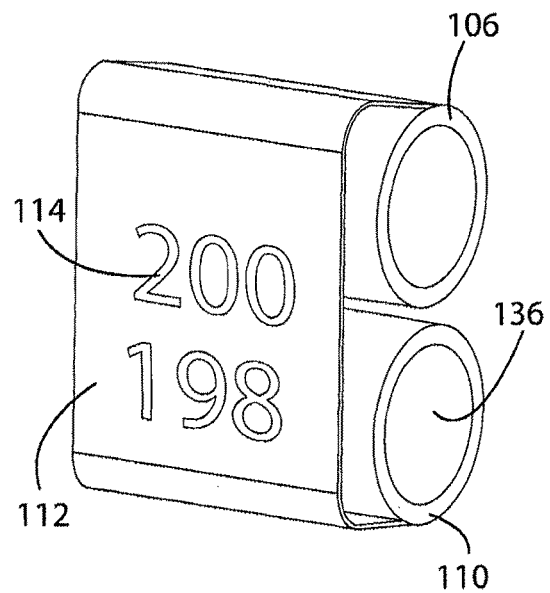


FIG. 6E

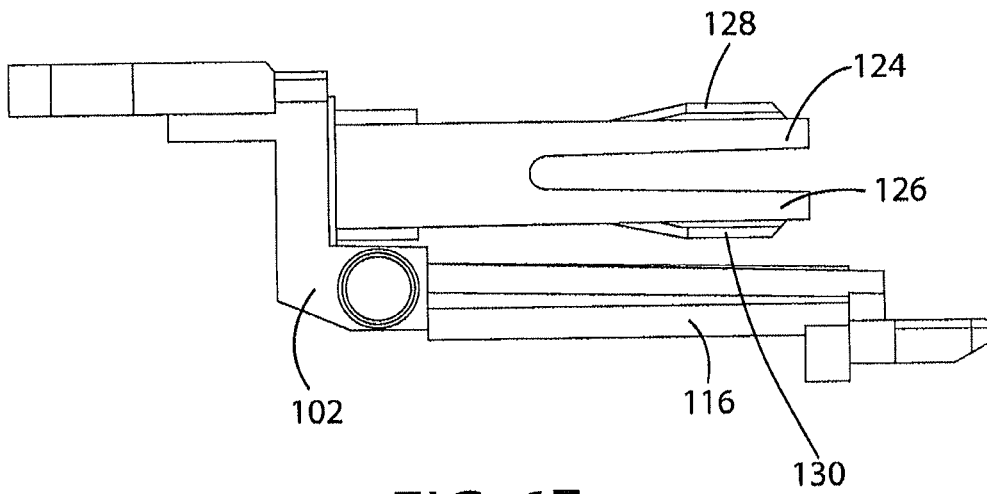


FIG. 6F

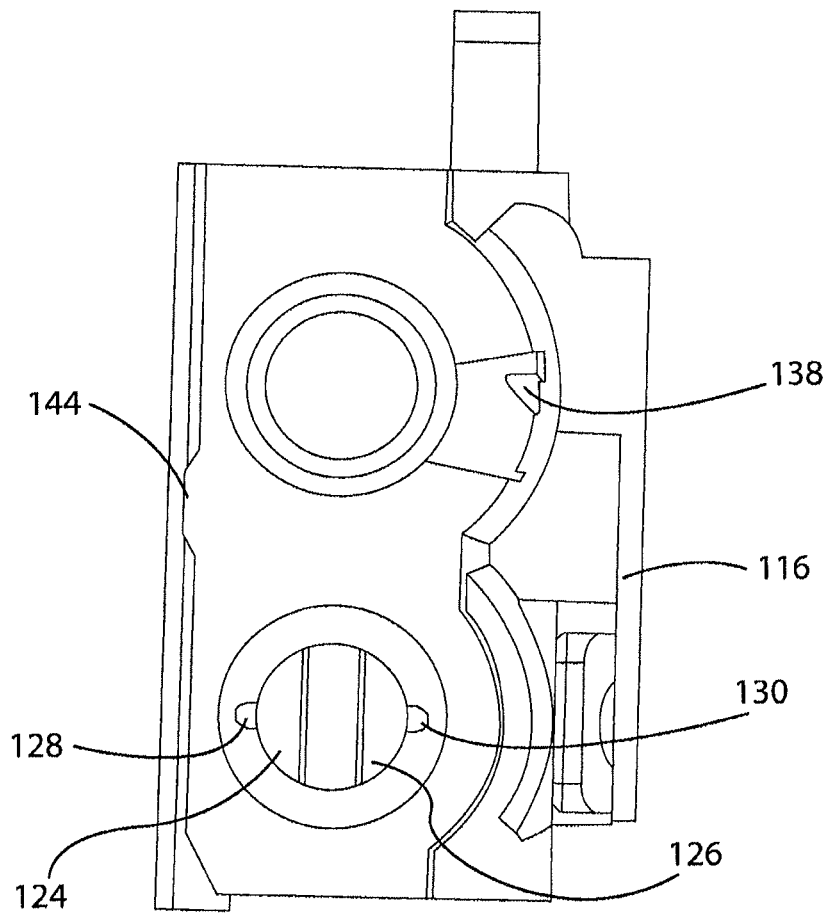


FIG. 6G

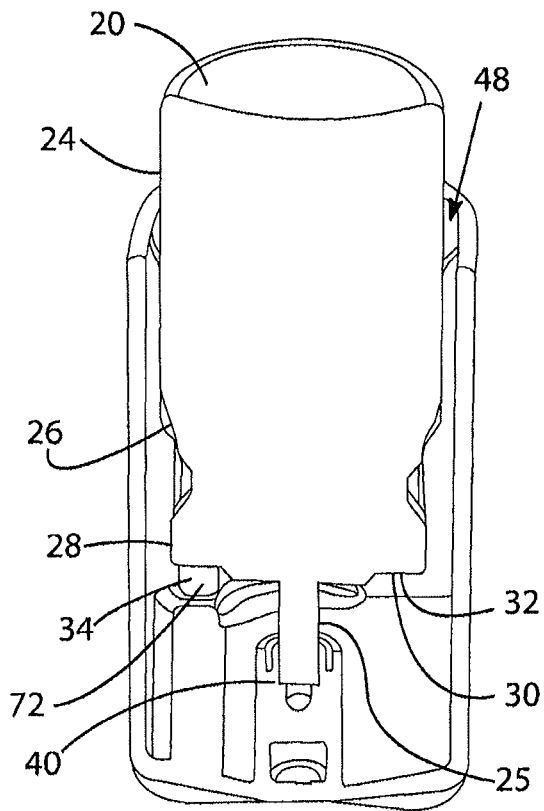


FIG. 7A

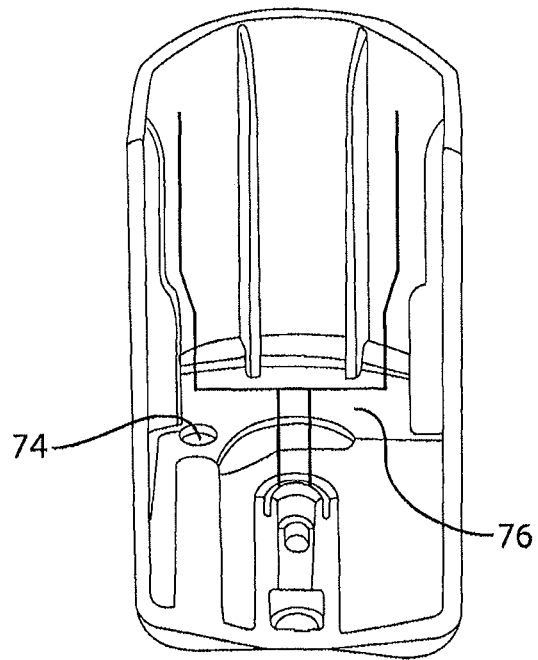


FIG. 7B

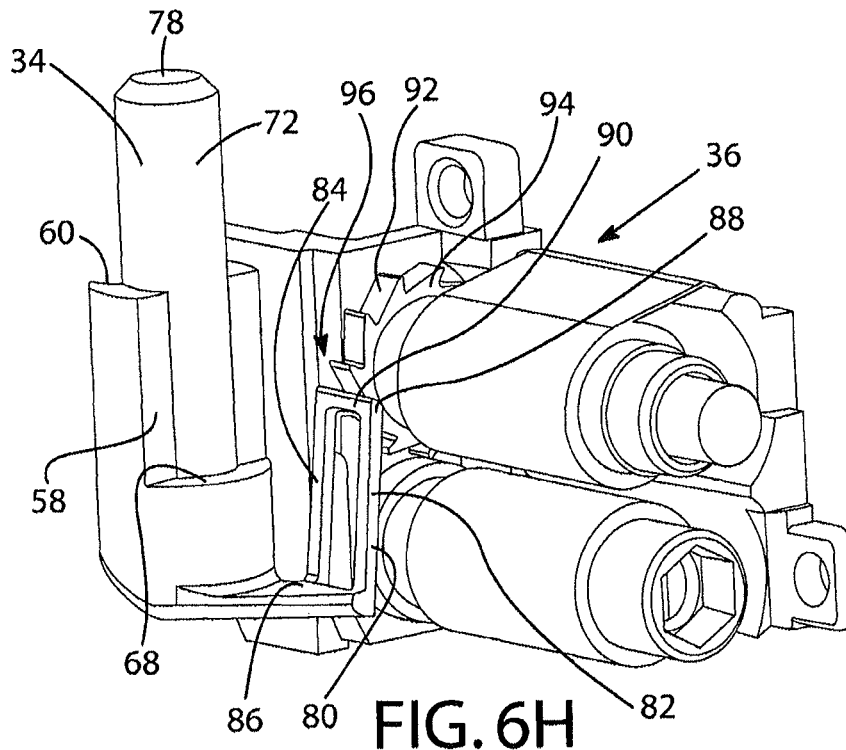
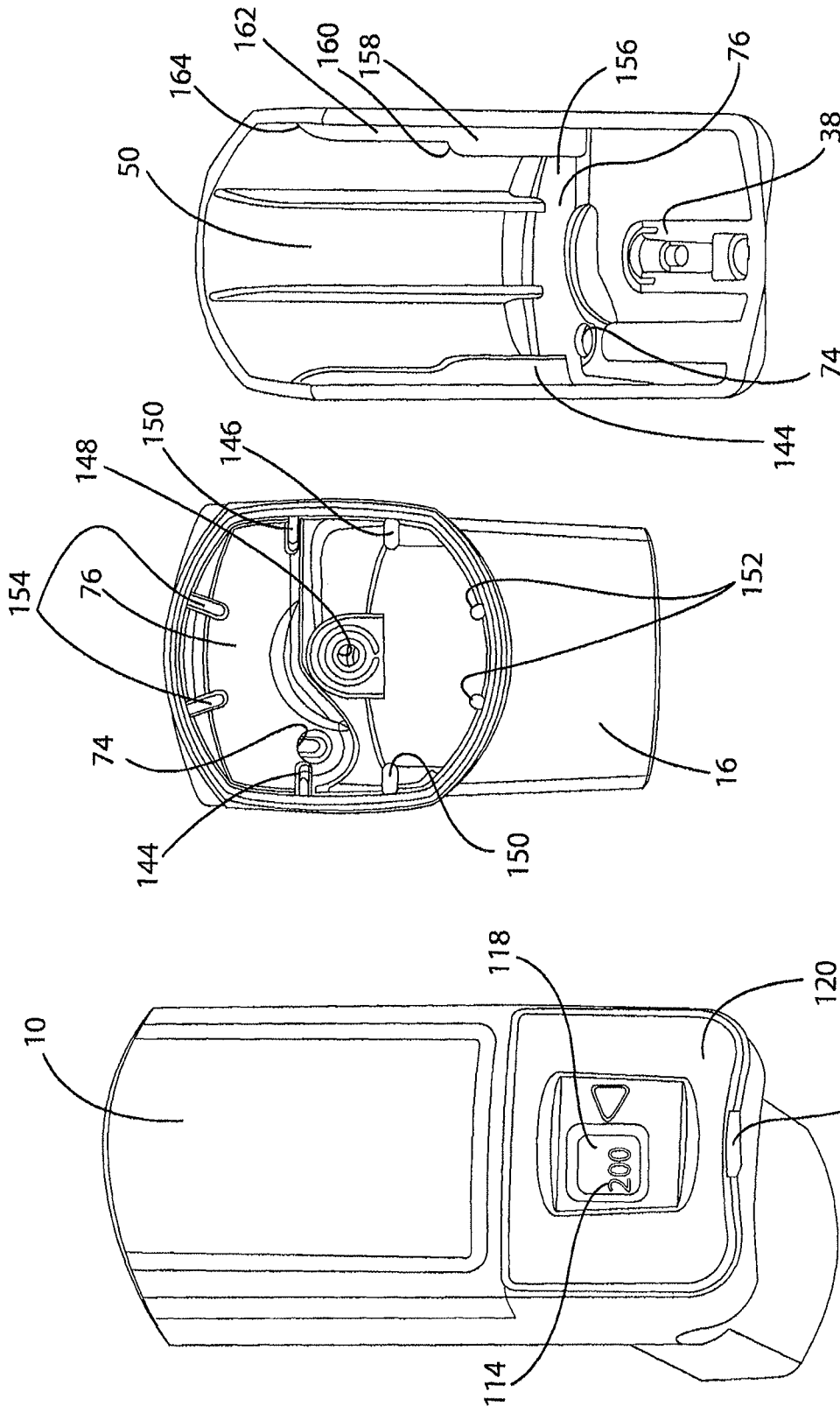


FIG. 6H

FIG. 8A



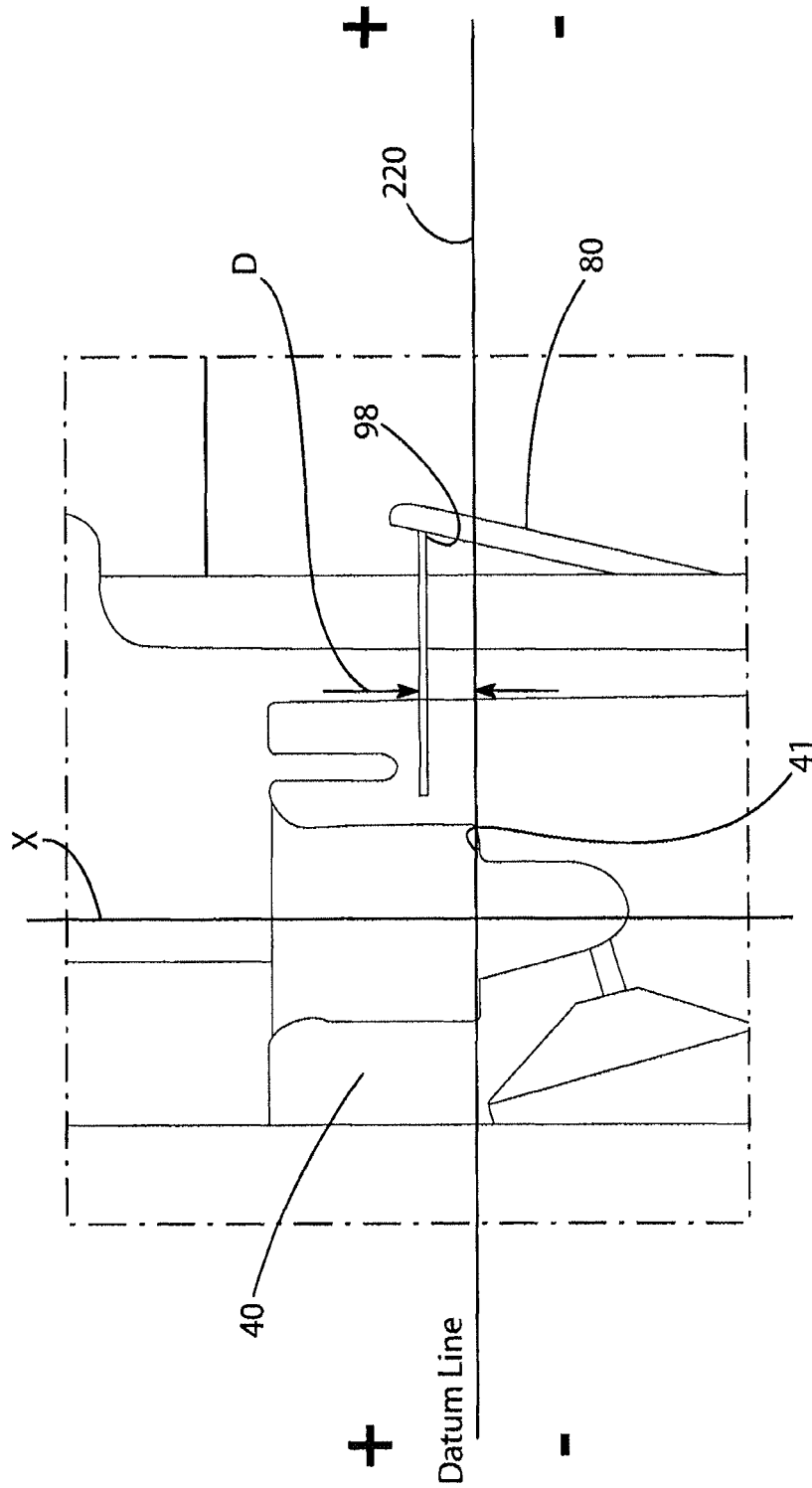
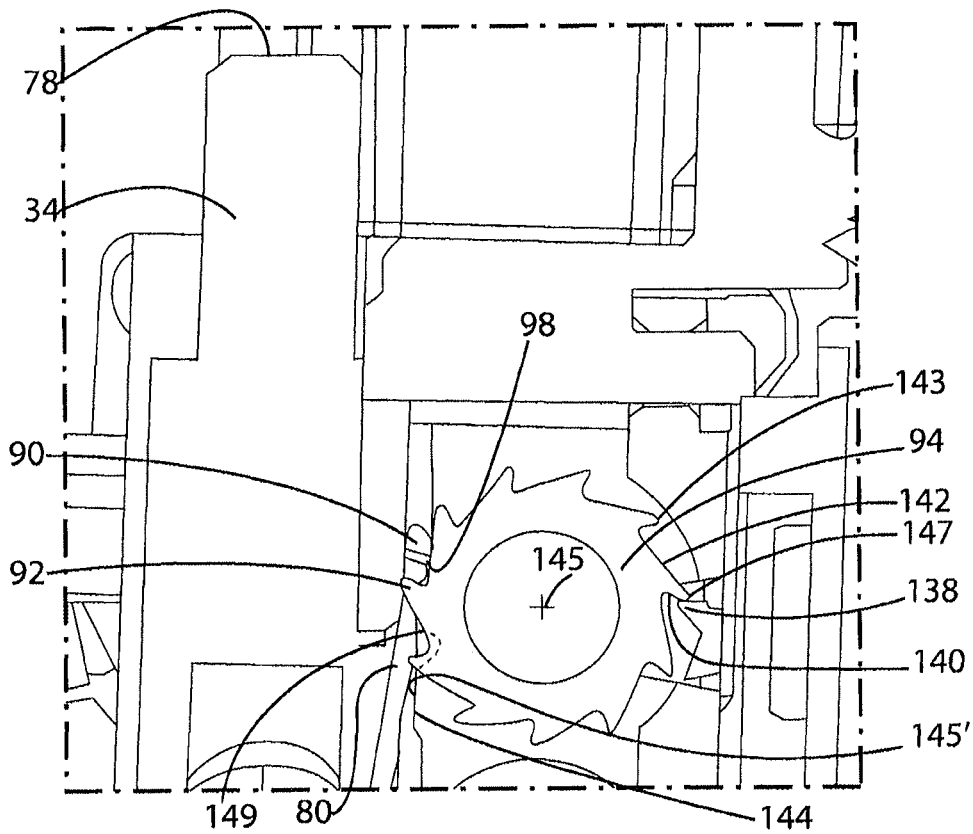
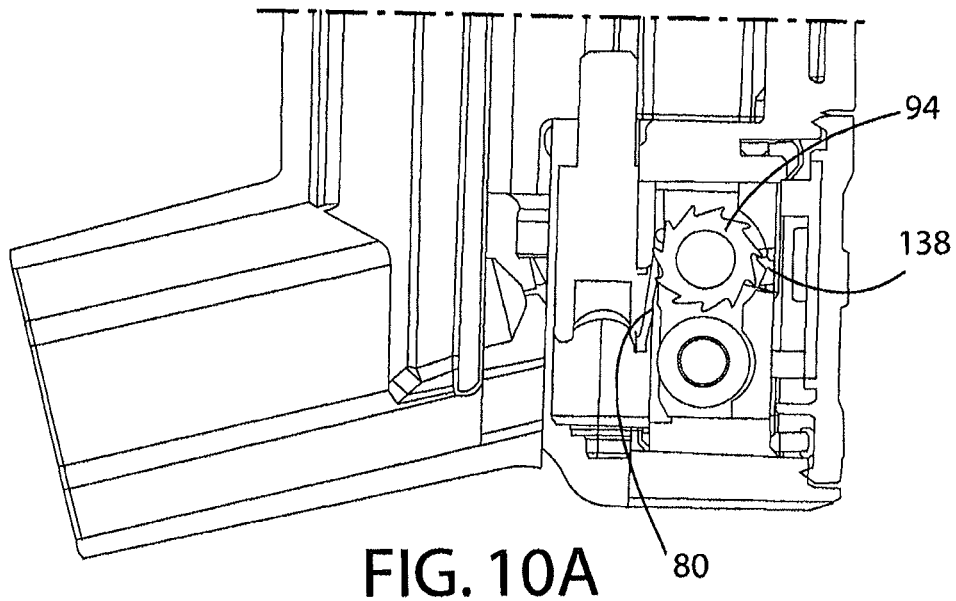


FIG. 9



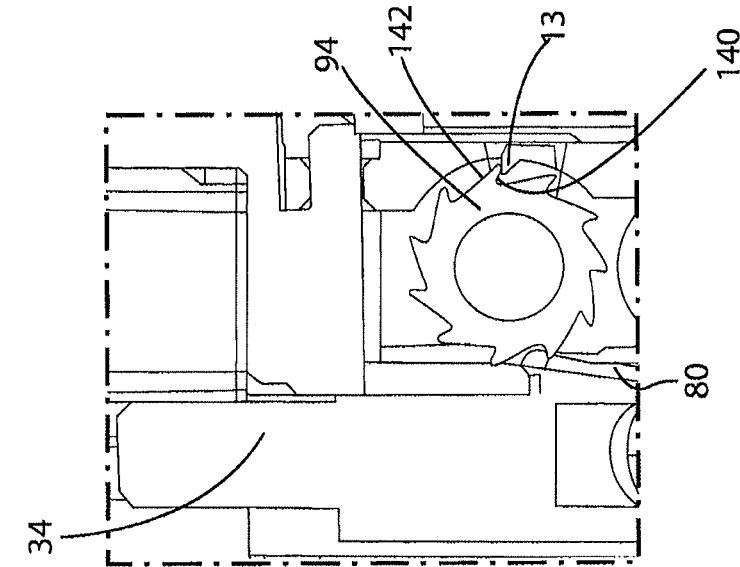


FIG. 10C

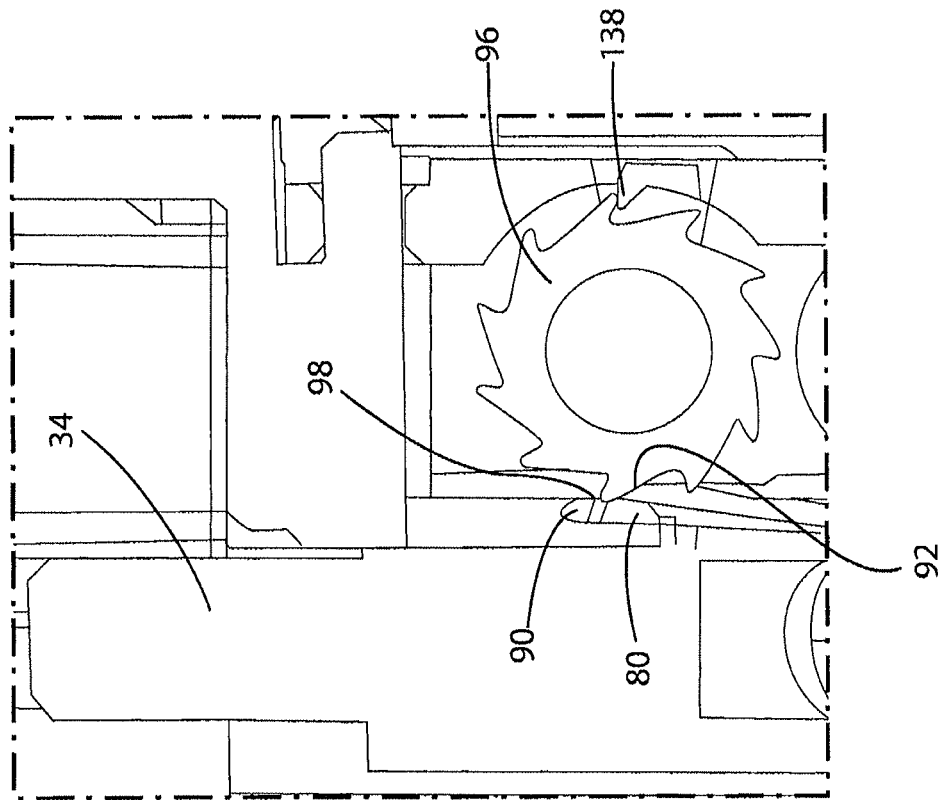


FIG. 10E

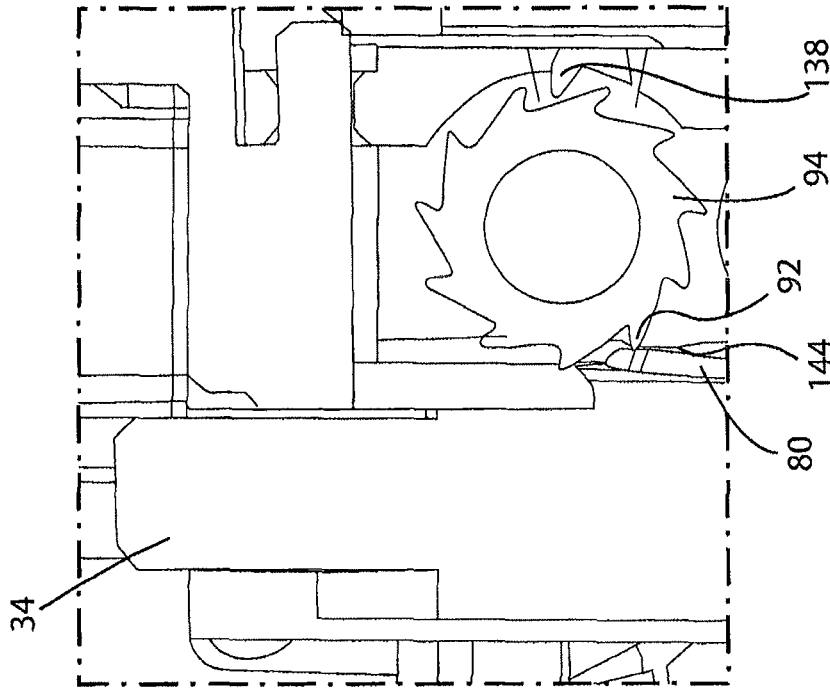


FIG. 10F

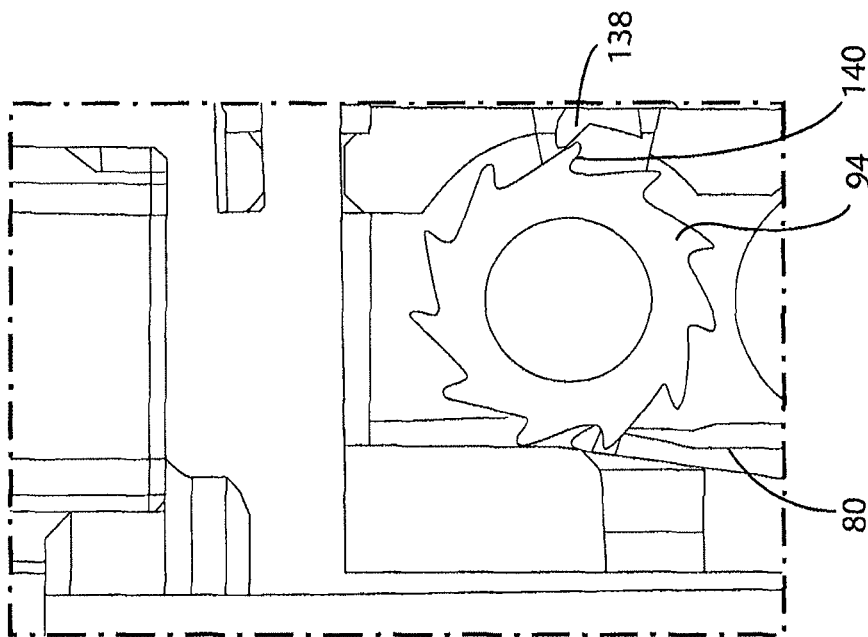


FIG. 10D

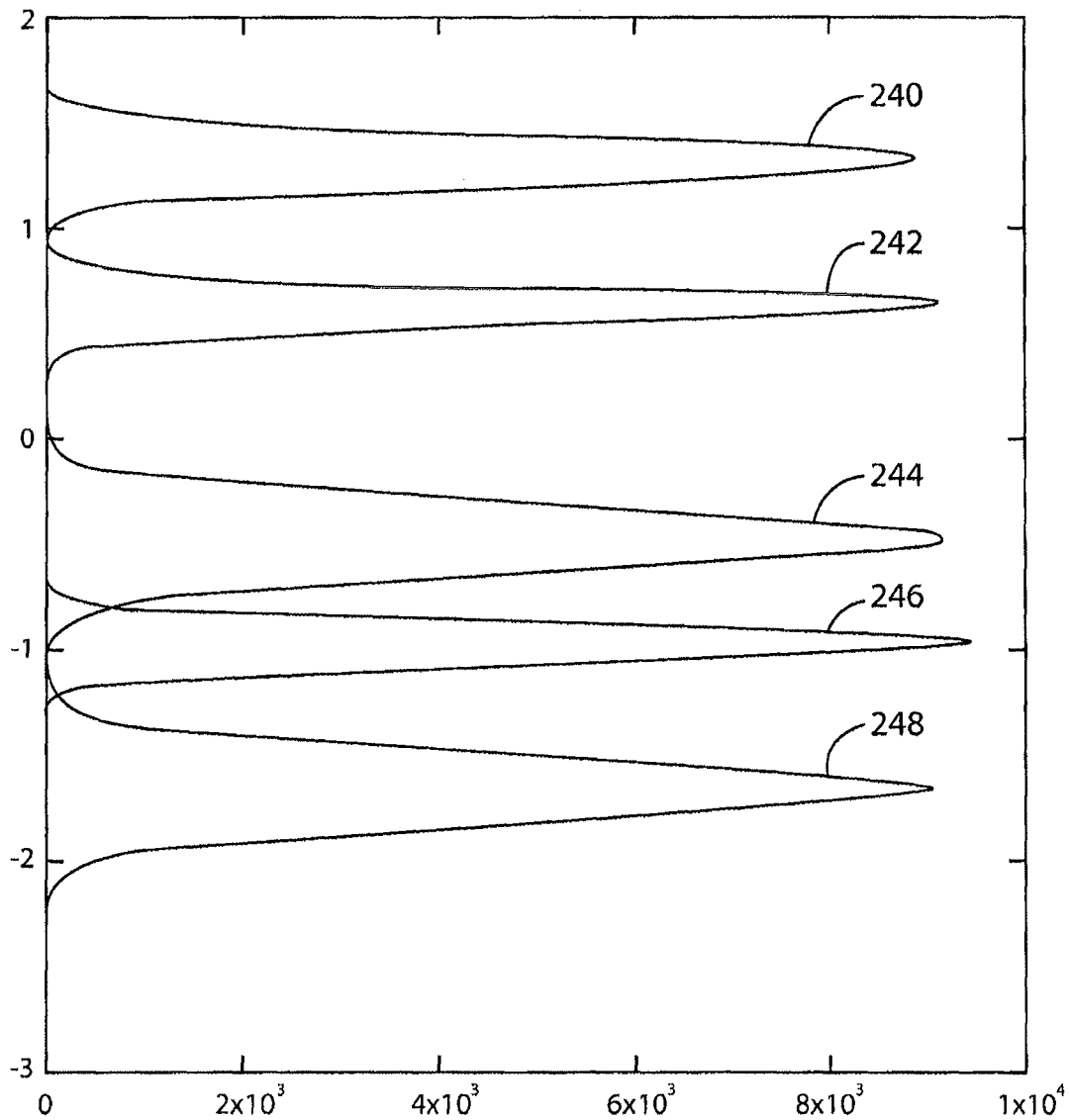


FIG. 11

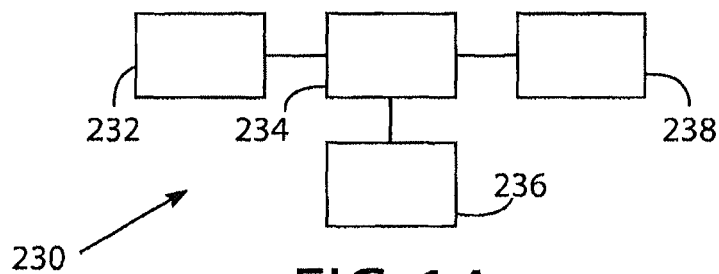


FIG. 14

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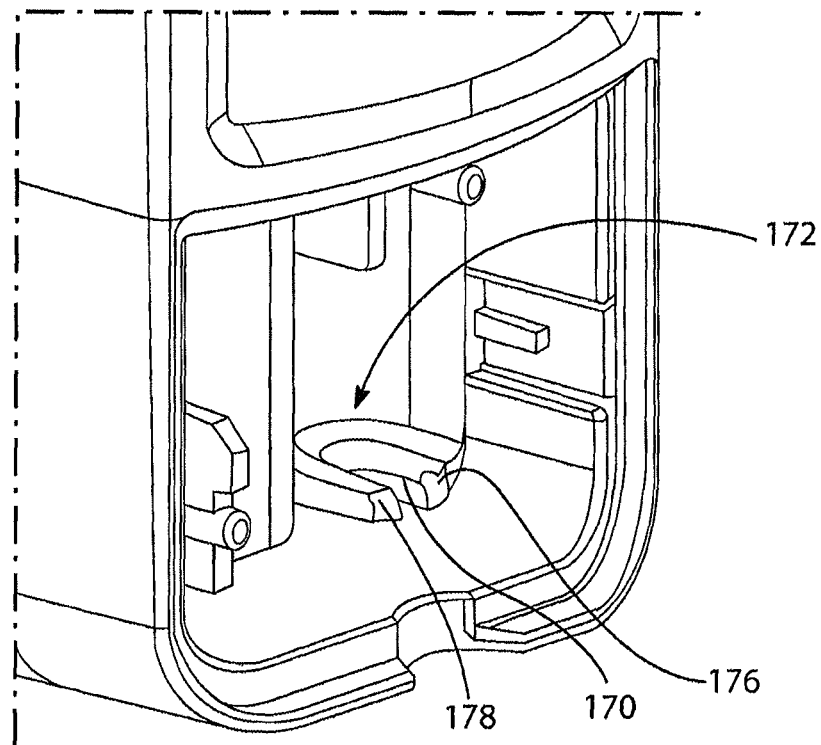


FIG. 12

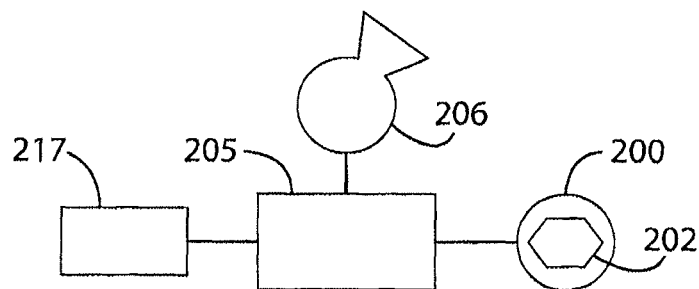
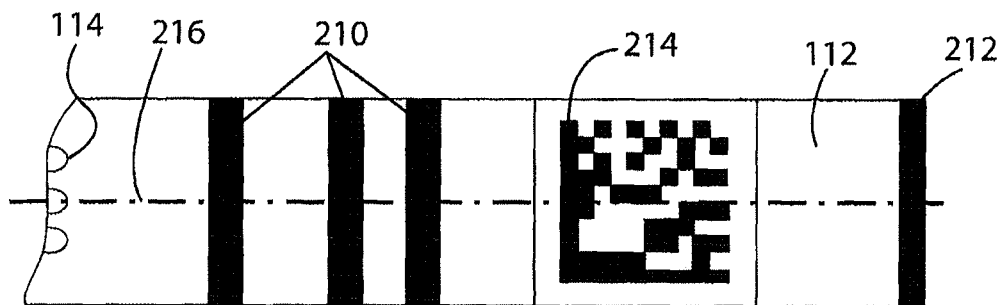


FIG. 13

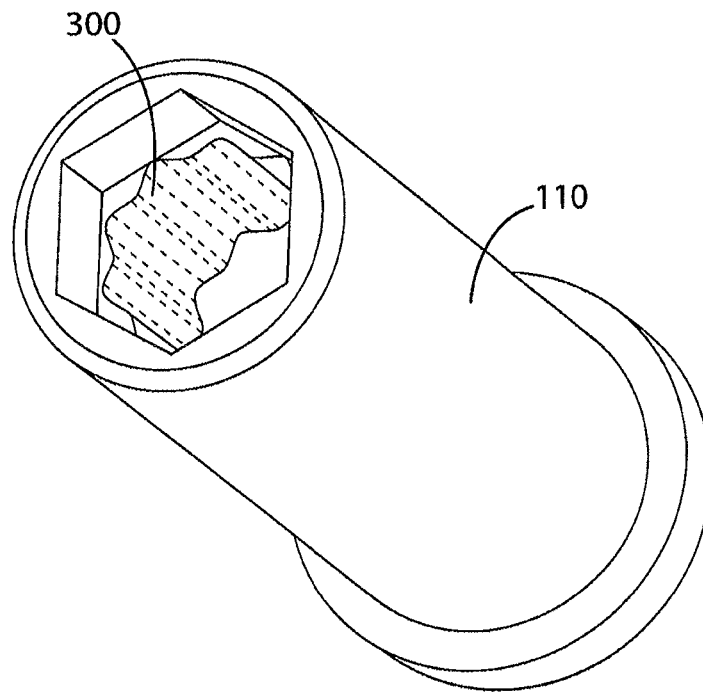


FIG. 15

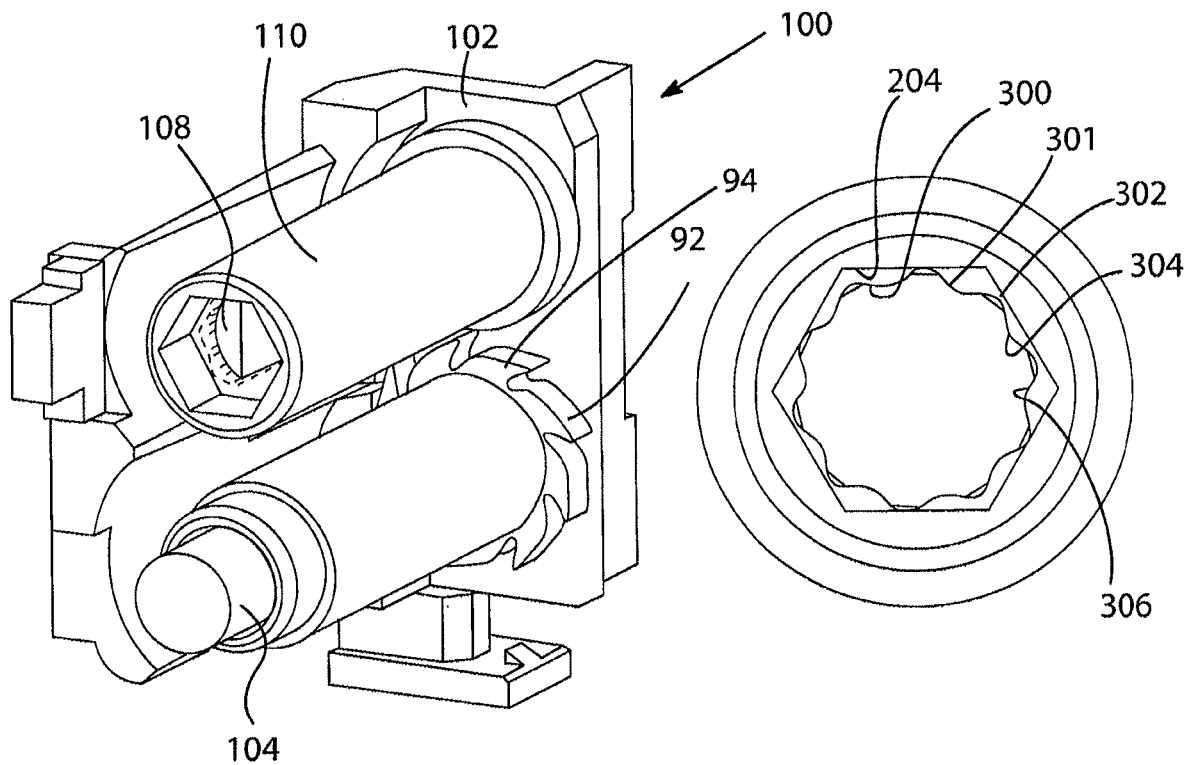


FIG. 20

FIG. 16

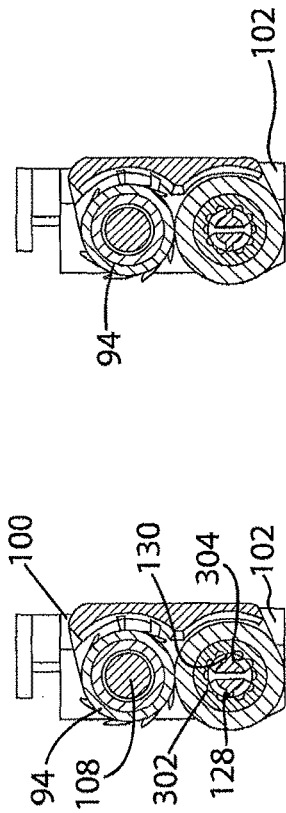


FIG. 18A

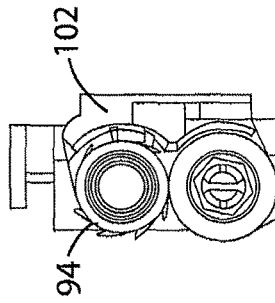


FIG. 18B

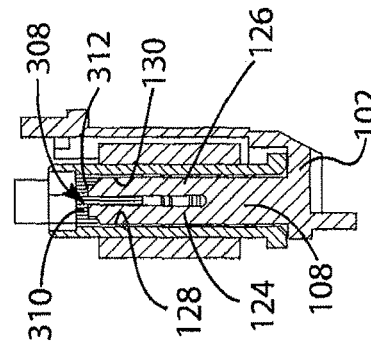


FIG. 18C

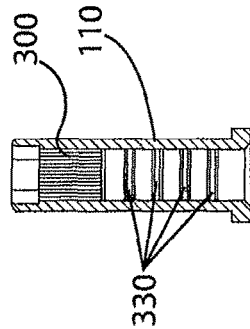


FIG. 17

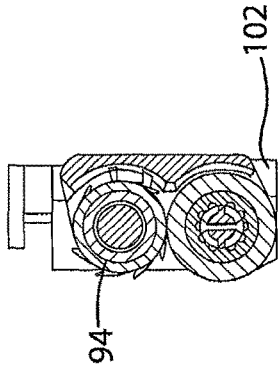


FIG. 19A

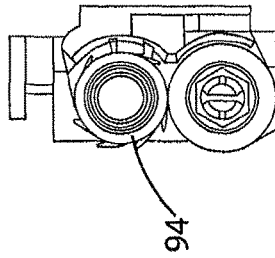


FIG. 19B

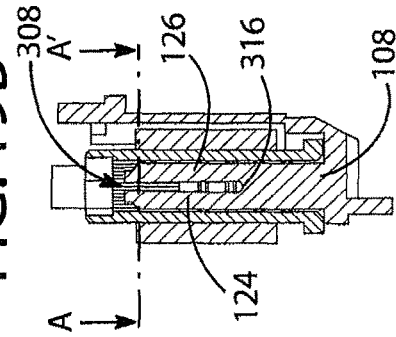


FIG. 19C

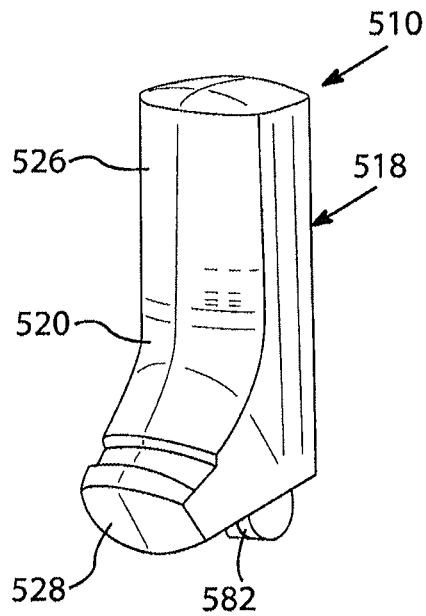


FIG. 21

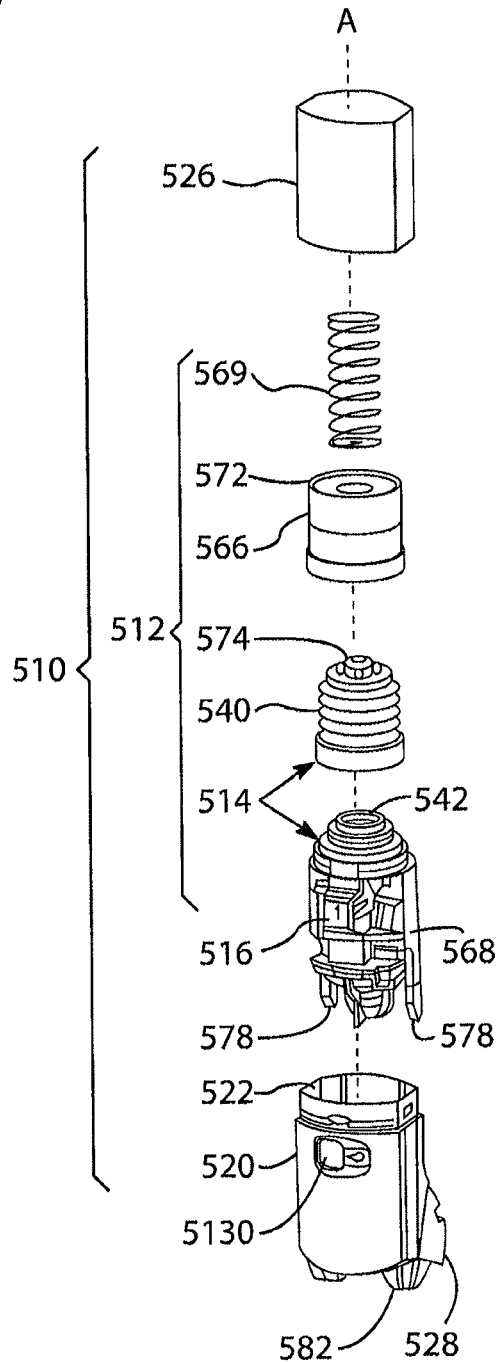


FIG. 22

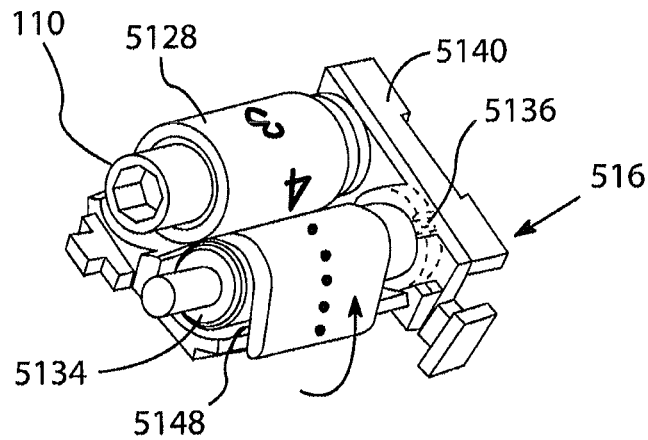


FIG. 23

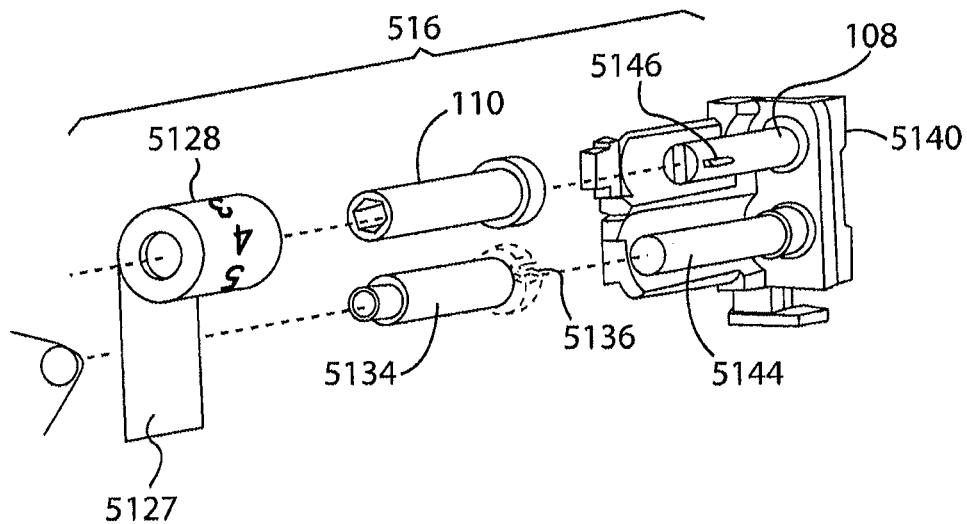


FIG. 24

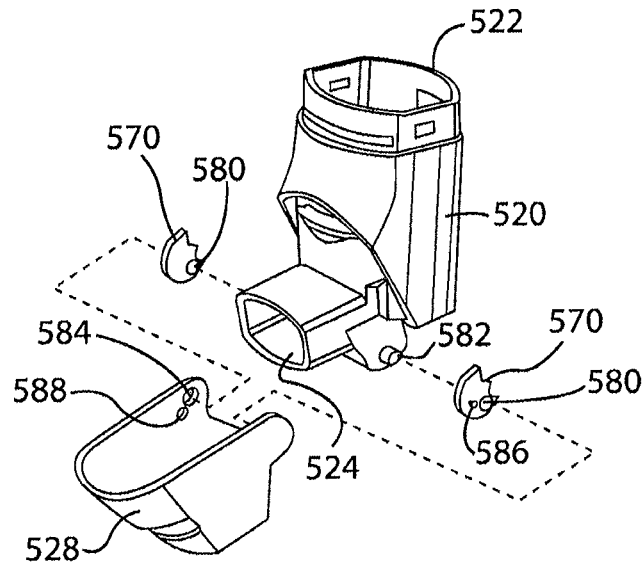


FIG. 25

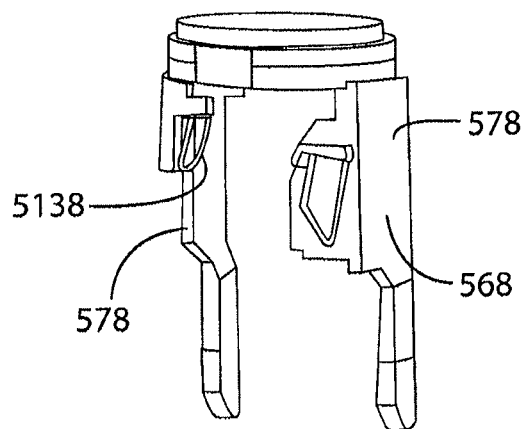


FIG. 26

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DOSE COUNTER FOR INHALER HAVING AN ANTI-REVERSE ROTATION ACTUATOR

CROSS-REFERENCE TO RELATED APPLICATIONS

This patent application is a continuation patent application of U.S. patent application Ser. No. 15/804,735 filed Nov. 6, 2017, which is a continuation of U.S. patent application Ser. No. 15/269,249, filed Sep. 19, 2016, now U.S. Pat. No. 9,808,587, which is a continuation of U.S. patent application Ser. No. 14/103,324, filed Dec. 11, 2013, now U.S. Pat. No. 9,463,289, which is a divisional patent application of U.S. patent application Ser. No. 13/110,532, filed May 18, 2011, now U.S. Pat. No. 8,978,966, which claims priority to U.S. Patent Application No. 61/345,763, filed May 18, 2010, and U.S. Patent Application No. 61/417,659, filed Nov. 29, 2010, each of which is incorporated herein by reference in its entirety for any and all purposes.

FIELD OF THE INVENTION

The present invention relates to dose counters for inhalers, inhalers and methods of assembly thereof. The invention is particularly applicable to metered dose inhalers including dry power medicament inhalers, breath actuated inhalers and manually operated metered dose medicament inhalers.

BACKGROUND OF THE INVENTION

Metered dose inhalers can comprise a medicament-containing pressurised canister containing a mixture of active drug and propellant. Such canisters are usually formed from a deep-drawn aluminium cup having a crimped lid which carries a metering valve assembly. The metering valve assembly is provided with a protruding valve stem which, in use is inserted as a push fit into a stem block in an actuator body of an inhaler having a drug delivery outlet. In order to actuate a manually operable inhaler, the user applies by hand a compressive force to a closed end of the canister and the internal components of the metering valve assembly are spring loaded so that a compressive force of approximately 15 to 30N is required to activate the device in some typical circumstances.

In response to this compressive force the canister moves axially with respect to the valve stem and the axial movement is sufficient to actuate the metering valve and cause a metered quantity of the drug and the propellant to be expelled through the valve stem. This is then released into a mouthpiece of the inhaler via a nozzle in the stem block, such that a user inhaling through the outlet of the inhaler will receive a dose of the drug.

A drawback of self-administration from an inhaler is that it is difficult to determine how much active drug and/or propellant are left in the inhaler, if any, especially of the active drug and this is potentially hazardous for the user since dosing becomes unreliable and backup devices not always available.

Inhalers incorporating dose counters have therefore become known.

WO 98/028033 discloses an inhaler having a ratchet mechanism for driving a tape drive dose counter. A shaft onto which tape is wound has a friction clutch or spring for restraining the shaft against reverse rotation.

EP-A-1486227 discloses an inhaler for dry powered medicament having a ratchet mechanism for a tape dose counter which is operated when a mouthpiece of the inhaler

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is closed. Due to the way in which the mouthpiece is opened and closed, and actuation pawl of the device which is mounted on a yoke, travels a known long stroke of consistent length as the mouthpiece is opened and closed.

WO 2008/119552 discloses a metered-dose inhaler which is suitable for breath-operated applications and operates with a known and constant canister stroke length of 3.04 mm+/-0.255 mm. A stock bobbin of the counter, from which a tape is unwound, rotates on a shaft having a split pin intended to hold the stock bobbin taut. However, some dose counters do not keep a particularly reliable count, such as if they are dropped onto a hard surface.

More recently, it has become desirable to improve dose counters further and, in particular, it is felt that it would be useful to provide extremely accurate dose counters for manually-operated canister-type metered dose inhalers. Unfortunately, in these inhalers, it has been found in the course of making the present invention that the stroke length of the canister is to a very large extent controlled on each dose operation by the user, and by hand. Therefore, the stroke length is highly variable and it is found to be extremely difficult to provide a highly reliable dose counter for these applications. The dose counter must not count a dose when the canister has not fired since this might wrongly indicate to the user that a dose has been applied and if done repeatedly the user would throw away the canister or whole device before it is really time to change the device due to the active drug and propellant reaching a set minimum. Additionally, the canister must not fire without the dose counter counting because the user may then apply another dose thinking that the canister has not fired, and if this is done repeatedly the active drug and/or propellant may run out while the user thinks the device is still suitable for use according to the counter. It has also been found to be fairly difficult to assembly some known inhaler devices and the dose counters therefor. Additionally, it is felt desirable to improve upon inhalers by making them easily usable after they have been washed with water.

The present invention aims to alleviate at least to a certain extent one or more of the problems of the prior art.

SUMMARY OF THE INVENTION

According to a first aspect of the present invention there is provided a dose counter for an inhaler, the dose counter having a counter display arranged to indicate dosage information, a drive system arranged to move the counter display incrementally in a first direction from a first station to a second station in response to actuation input, wherein a regulator is provided which is arranged to act upon the counter display at the first station to regulate motion of the counter display at the first station to incremental movements.

The regulator is advantageous in that it helps prevent unwanted motion of the counter display if the counter is dropped.

According to a further aspect of the present invention, the regulator provides a resistance force of greater than 0.1 N against movement of the counter display. According to still a further aspect of the present invention, the resistance force is greater than 0.3 N. According to yet a further aspect of the present invention, the resistance force is from 0.3 to 0.4 N.

Preferably, the counter comprises a tape.

Preferably, the tape has dose counter indicia displayed thereon. The first station may comprise a region of the dose counter where tape is held which is located before a display location, such as a display window, for the counter indicia.

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The first station may comprise a first shaft, the tape being arranged on the first shaft and to unwind therefrom upon movement of the counter display.

The first shaft may be mounted for rotation relative to a substantially rotationally fixed element of the dose counter.

The regulator may comprise at least one projection which is arranged on one of the first shaft and the substantially rotationally fixed element and to engage incrementally with one or more formations on the other of the first shaft and the substantially rotationally fixed element.

At least two said projections may be provided. Exactly two said projections may be provided.

Each projection may comprise a radiused surface.

The at least one projection may be located on the substantially fixed element which may comprise a fixed shaft which is fixed to a main body of the dose counter, the first shaft being rotationally mounted to the fixed shaft.

Preferably, the fixed shaft has at least two resiliently flexible legs (or forks). Each leg may have at least one said projection formed in an outwardly facing direction thereon, said one or more formations being formed on an inwardly facing engagement surface of the first shaft, said at least one projection being arranged to resiliently engage said one or more formations. Preferably, a series of said formations are provided. An even number of said formations may be provided. Eight to twelve of said formations may be provided. In one embodiment, ten said formations are provided.

Each said formation may comprise a concavity formed on an engagement surface. Each concavity may comprise a radiused surface wall portion which preferably merges on at least one side thereof into a flat wall portion surface. The engagement surface may include a series of said concavities, and convex wall portions of the engagement surface may be formed between each adjacent two said concavities, each said convex wall portion comprising a convex radiused wall portion.

Each convex radiused wall portion of each convex wall portion may be connected by said flat wall portion surfaces to each adjacent concavity.

The fixed shaft may comprise a split pin with fork legs and each projection may be located on a said fork leg.

The first shaft may comprise a substantially hollow bobbin.

Said at least one formation may be located on an inner surface of the bobbin. In other embodiments it may be located on an outer surface thereof. Said engagement surface may extend partially along said bobbin, a remainder of the respective inner or outer surface having a generally smooth journal portion along at least a portion thereof.

The drive system may comprise a tooth ratchet wheel arranged to act upon a second shaft which is located at the second station, the second shaft being rotatable to wind the tape onto the second shaft.

The second shaft may be located on a main body of the dose counter spaced from and parallel to the first shaft.

The ratchet wheel may be fixed to the second shaft is arranged to rotate therewith. The ratchet wheel may be secured to an end of the second shaft and aligned coaxially with the second shaft.

The dose counter may include anti-back drive system which is arranged to restrict motion of the second shaft. The anti-back drive system may include a substantially fixed tooth arranged to act upon teeth of the ratchet wheel.

According to a further aspect of the present invention, a dose counter includes an anti-back drive system which is arranged to restrict motion of the second shaft in a tape winding direction.

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According to a further aspect of the present invention there is provided a shaft for holding counter tape in a dose counter for an inhaler, the shaft having an engagement surface including incrementally spaced formations located around a periphery thereof, the formations comprising a series of curved concavities and convex portions.

The shaft may comprise a hollow bobbin.

The engagement surface may be a generally cylindrical inwardly directed surface.

The engagement surface may include a flat surface wall portion joining each concavity and convex wall portion.

Each concavity may comprise a radiused wall portion.

Each convex wall portion may comprise a radiused wall portion.

Said concavities may be regularly spaced around a longitudinal axis of the shaft.

Said convex wall portions may be regularly spaced around a longitudinal axis of the shaft.

In some embodiments there may be from eight to twelve said concavities and/or convex wall portions regularly spaced around a longitudinal axis thereof.

One embodiment includes ten said concavities and/or convex wall portions regularly spaced around a longitudinal axis of the shaft.

According to a further aspect of the present invention there is provided a shaft and counter tape assembly for use in a dose counter for an inhaler, the assembly comprising a rotatable shaft and a counter tape which is wound around the shaft and is adapted to unwind therefrom upon inhaler actuation, the shaft having an engagement surface which includes incrementally spaced formations located around a periphery thereof.

According to a further aspect of the present invention there is provided an inhaler for the inhalation of medication and the like, the inhaler including a dose counter as in the first aspect of the present invention.

A preferred construction consists of a manually operated metered dose inhaler including a dose counter chamber including a dose display tape driven by a ratchet wheel which is driven in turn by an actuator pawl actuated by movement of a canister, the tape unwinding from a stock bobbin during use of the inhaler, a rotation regulator being provided for the stock bobbin and comprising a wavelike engagement surface with concavities which engage against control elements in the form of protrusions on resilient forks of a split pin thereby permitting incremental unwinding of the stock bobbin yet resisting excessive rotation if the inhaler is dropped onto a hard surface.

According to another aspect of the present invention there is provided a dose counter for a metered dose inhaler having a body arranged to retain a medicament canister of predetermined configuration for movement of the canister relative thereto; the dose counter comprising: an incremental counting system for counting doses, the incremental counting system having a main body, an actuator arranged to be driven in response to canister motion and to drive an incremental output member in response to canister motion, the actuator and incremental output member being configured to have predetermined canister fire and count configurations in a canister fire sequence, the canister fire configuration being determined by a position of the actuator relative to a datum at which the canister fires medicament and the count configuration being determined by a position of the actuator relative to the datum at which the incremental count system makes an incremental count, wherein the actuator is

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arranged to reach a position thereof in the count configuration at or after a position thereof in the canister fire configuration.

This arrangement has been found to be highly advantageous since it provides an extremely accurate dose counter which is suitable for use with manually operated metered dose inhalers. It has been found that dose counters with these features have a failure rate of less than 50 failed counts per million full canister activation depressions. It has been found in the course of making the present invention that highly reliable counting can be achieved with the dose counter counting at or soon after the point at which the canister fires. It has been is covered by the present inventors that momentum and motion involved in firing the canister, and in some embodiments a slight reduction in canister back pressure on the user at the time of canister firing, can very reliably result in additional further motion past the count point.

The actuator and incremental counting system may be arranged such that the actuator is displaced less than 1 mm, typically 0.25 to 0.75 mm, more preferably about 0.4 to 0.6 mm, relative to the body between its location in the count and fire configurations, about 0.48 mm being preferred. The canister, which can move substantially in line with the actuator, can reliably move this additional distance so as to achieve very reliable counting.

The incremental count system may comprise a ratchet mechanism and the incremental output member may comprise a ratchet wheel having a plurality of circumferentially spaced teeth arranged to engage the actuator.

The actuator may comprise an actuator pawl arranged to engage on teeth of the ratchet wheel. The actuator pawl may be arranged to be connected to or integral with an actuator pin arranged to engage and be depressed by a medicament canister bottom flange. The actuator pawl may be generally U-shaped having two parallel arms arranged to pull on a central pawl member arranged substantially perpendicular thereto. This provides a very reliable actuator pawl which can reliably pull on the teeth of the ratchet wheel.

The incremental count system may include a tape counter having tape with incremental dose indicia located thereon, the tape being positioned on a tape stock bobbin and being arranged to unwind therefrom.

The actuator and incremental output member may be arranged to provide a start configuration at which the actuator is spaced from the ratchet output member, a reset configuration at which the actuator is brought into engagement with the incremental output member during a canister fire sequence, and an end configuration at which the actuator disengages from the ratchet output during a canister fire sequence.

The actuator may be arranged to be located about 1.5 to 2.0 mm, from its location in the fire configuration, when in the start configuration, about 1.80 mm being preferred.

The actuator may be arranged to be located about 1.0 to 1.2 mm, from its location in the fire configuration, when in the reset configuration, about 1.11 mm being preferred.

The actuator may be arranged to be located about 1.1 to 1.3 mm, from its location in the fire configuration, when in the end configuration, about 1.18 mm being preferred.

These arrangements provide extremely reliable dose counting, especially with manually operated canister type metered dose inhalers.

The main body may include a formation for forcing the actuator to disengage from the incremental output member when the actuator is moved past the end configuration. The formation may comprise a bumped up portion of an other-

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wise generally straight surface against which the actuator engages and along which it is arranged to slide during a canister firing sequence.

The dose counter may include a counter pawl, the counter pawl having a tooth arranged to engage the incremental output member, the tooth and incremental output member being arranged to permit one way only incremental relative motion therebetween. When the incremental output member comprises a ratchet wheel, the tooth can therefore serve as an anti-back drive tooth for the ratchet wheel, thereby permitting only one way motion or rotation thereof.

The counter pawl may be substantially fixedly mounted on the main body of the incremental count system and the counter pawl may be arranged to be capable of repeatedly engaging equi-spaced teeth of the incremental output member in anti-back drive interlock configurations as the counter is operated. The counter pawl may be positioned so that the incremental output member is halfway, or substantially halfway moved from one anti-back drive interlock configuration to the next when the actuator and incremental output member are in the end configuration thereof. This is highly advantageous in that it minimises the risk of double counting or non-counting by the dose counter.

According to a further aspect of the invention there is provided an inhaler comprising a main body arranged to retain a medicament canister of predetermined configuration and a dose counter mounted in the main body.

The inhaler main body may include a canister receiving portion and a separate counter chamber, the dose counter being located within the main body thereof, the incremental output member and actuator thereof inside the counter chamber, the main body of the inhaler having wall surfaces separating the canister-receiving portion and the counter chamber, the wall surfaces being provided with a communication aperture, an actuation member extending through the communication aperture to transmit canister motion to the actuator.

According to a further aspect of the present invention there is a provided an inhaler for metered dose inhalation, the inhaler comprising a main body having a canister housing arranged to retain a medicament canister for motion therein, and a dose counter, the dose counter having an actuation member having at least a portion thereof located in the canister housing for operation by movement of a medicament canister, wherein the canister housing has an inner wall, and a first inner wall canister support formation located directly adjacent the actuation member.

This is highly advantageous in that the first inner wall canister support formation can prevent a canister from rocking too much relative to the main body of the inhaler. Since the canister may operate the actuation member of the dose counter, this substantially improves dose counting and avoids counter errors.

The canister housing may have a longitudinal axis which passes through a central outlet port thereof, the central outlet port being arranged to mate with an outer canister fire stem of a medicament canister, the inner wall canister support formation, the actuation member and the outlet port lying in a common plane coincident with the longitudinal axis. Accordingly, this construction may prevent the canister from rocking towards the position of the dose counter actuation member, thereby minimising errors in counting.

The canister housing may have a further inner canister wall support formation located on the inner wall opposite, or substantially opposite, the actuation member. Accordingly, the canister may be supported against rocking motion away from the actuator member so as to minimise count errors.

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The canister housing may be generally straight and tubular and may have an arrangement in which each said inner wall support formation comprises a rail extending longitudinally along the inner wall.

Each said rail may be stepped, in that it may have a first portion located towards a medicine outlet end or stem block of the canister housing which extends inwardly a first distance from a main surface of the inner wall and a second portion located toward an opposite end of the canister chamber which extends inwardly a second, smaller distance from the main surface of the inner wall. This may therefore enable easy insertion of a canister into the canister housing such that a canister can be lined up gradually in step wise function as it is inserted into the canister housing.

The inhaler may include additional canister support rails which are spaced around an inner periphery of the inner wall of the canister housing and which extend longitudinally therealong.

At least one of the additional rails may extend a constant distance inwardly from the main surface of the inner wall.

At least one of the additional rails may be formed with a similar configuration to the first inner wall canister support formation.

The dose counter may, apart from said at least a portion of the actuation member, be located in a counter chamber separate from the canister housing, the actuation member comprising a pin extending through an aperture in a wall which separates the counter chamber and the canister housing.

According to a further aspect of the present invention there is provided an inhaler for inhaling medicaments having: a body for retaining a medicament store; the body including a dose counter, the dose counter having a moveable actuator and a return spring for the actuator, the return spring having a generally cylindrical and annular end; the body having a support formation therein for supporting said end of the return spring, the support formation comprising a shelf onto which said end is engageable and a recess below the shelf.

This shelf and recess arrangement is highly advantageous since it allows a tool (such as manual or mechanical tweezers) to be used to place the return spring of the actuator onto the shelf with the tool then being withdrawn at least partially via the recess.

The shelf may be U-shaped.

The support formation may include a U-shaped upstanding wall extending around the U-shaped shelf, the shelf and upstanding wall thereby forming a step and riser of a stepped arrangement.

The recess below the shelf may also be U-shaped.

At least one chamfered surface may be provided at an entrance to the shelf. This may assist in inserting the actuator and return spring into position.

A further aspect of the invention provides a method of assembly of an inhaler which includes the step of locating said end of said spring on the shelf with an assembly tool and then withdrawing the assembly tool at least partly via the recess. This assembly method is highly advantageous compared to prior art methods in which spring insertion has been difficult and in which withdrawal of the tool has sometimes accidentally withdrawn the spring again.

The cylindrical and annular end of the spring may be movable in a direction transverse to its cylindrical extent into the shelf while being located thereon.

According to a further aspect of the present invention there is provided an inhaler for inhaling medicament, the inhaler having a body for retaining a medicament store; and

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a dose counter, the dose counter having a moveable actuator and a chassis mounted on the body; the chassis being heat staked in position on the body. This is highly advantageous in that the chassis can be very accurately positioned and held firmly in place, thereby further improving counting accuracy compared to prior art arrangements in which some movement of the chassis relative to the body may be tolerated in snap-fit connections.

The chassis may have at least one of a pin or aperture heat staked to a respective aperture or pin of the body.

The chassis may have a ratchet counter output member mounted thereon.

The ratchet counter output member may comprise a ratchet wheel arranged to reel in incrementally a dose meter tape having a dosage indicia located thereon.

According to a further aspect of the present invention there is provided a method of assembling an inhaler including the step of heat staking the chassis onto the body. The step of heat staking is highly advantageous in fixedly positioning the chassis onto the body in order to achieve highly accurate dose counting in the assembled inhaler.

The method of assembly may include mounting a spring-returned ratchet actuator in the body before heat staking the chassis in place. The method of assembly may include pre-assembling the chassis with a dose meter tape prior to the step of heat staking the chassis in place. The method of assembly may include attaching a dose meter cover onto the body after the heat staking step. The cover may be welded onto the body or may in some embodiments be glued or otherwise attached in place.

According to a further aspect of the present invention there is provided an inhaler for inhaling medicament and having a body, the body have a main part thereof for retaining a medicament store; and a dose counter, the dose counter being located in a dose counter chamber of the body which is separated from the main part of the body, the dose counter chamber of the body having a dosage display and being perforated so as to permit the evaporation of water or aqueous matter in the dose counter chamber into the atmosphere.

This is high advantageous since it enables the inhaler to be thoroughly washed and the dose counting chamber can thereafter dry out fully.

The display may comprise a mechanical counter display inside the dose counter chamber and a window for viewing the mechanical counter display. The mechanical counter display may comprise a tape. The perforated dose counter chamber may therefore enable reliable washing of the inhaler, if desired by the user, and may therefore dry out without the display window misting up.

The dose counter chamber may be perforated by a drain hole formed through an outer hole of the body. The drain hole may be located at a bottom portion of the body of the inhaler, thereby enabling full draining of the inhaler to be encouraged after washing when the inhaler is brought into an upright position.

According to a further aspect of the present invention there is provided a dose counter for an inhaler, the dose counter having a display tape arranged to be incrementally driven from a tape stock bobbin onto an incremental tape take-up drive shaft, the bobbin having an internal bore supported by and for rotation about a support shaft, at least one of the bore and support shaft having a protrusion which is resiliently biased into frictional engagement with the other of the bore and support shaft with longitudinally extending mutual frictional interaction. This arrangement may provide good friction for the bobbin, thereby improving tape counter

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display accuracy and preventing the bobbin from unwinding undesirably for example if the inhaler is accidentally dropped.

The support shaft may be forked and resilient for resiliently biasing the support shaft and bore into frictional engagement.

The support shaft may have two forks, or more in some cases, each having a radially extending protrusion having a friction edge extending therealong parallel to a longitudinal axis of the support shaft for frictionally engaging the bore of the support shaft with longitudinally extending frictional interaction therebetween.

The bore may be a smooth circularly cylindrical or substantially cylindrical bore.

Each of the above inhalers in accordance with aspects of the present invention may have a medicament canister mounted thereto.

The canister may comprise a pressurised metered dose canister having a reciprocally movable stem extending therefrom and movable into a main canister portion thereof for releasing a metered dose of medicament under pressure, for example by operating a metered dose valve inside the canister body. The canister may be operable by pressing by hand on the main canister body.

In cases in which one or more support rails or inner wall support formations are provided, the canister may at all times when within the canister chamber have a clearance of about 0.25 to 0.35 mm from the first inner wall support formation. The clearance may be almost exactly 0.3 mm. This clearance which may apply to the canister body itself or to the canister once a label has been applied, is enough to allow smooth motion of the canister in the inhaler while at the same time preventing substantial rocking of the canister which could result in inaccurate counting by a dose counter of the inhaler, especially when lower face of the canister is arranged to engage an actuator member of the dose counter for counting purposes.

According to a further aspect of the invention, a method of assembling a dose counter for an inhaler comprises the steps of providing a tape with dosing indicia thereon; providing tape positioning indicia on the tape; and stowing the tape while monitoring for the tape positioning indicia with a sensor. The method advantageously permits efficient and accurate stowing of the tape, e.g. by winding.

The dosing indicia may be provided as numbers, the tape positioning indicia may be provided as one or more lines across the tape. The stowing step comprises winding the tape onto a bobbin or shaft, and, optionally, stopping winding when the positioning indicia are in a predetermined position. The tape may be provided with pixelated indicia at a position spaced along the tape from the positioning indicia.

The tape may also be provided with a priming dot.

According to a further aspect of the invention, a tape system for a dose counter for an inhaler has a main elongate tape structure, and dosing indicia and tape positioning indicia located on the tape structure. The tape positioning indicia may comprise at least one line extending across the tape structure. The tape system may comprise pixelated indicia located on the tape structure and spaced from the positioning indicia. The tape system may comprise a priming dot located on the tape structure. The positioning indicia may be located between the timing dot and the pixelated indicia. The main elongate tape structure may have at least one end thereof wound on a bobbin or shaft.

A further aspect of the invention provides a method of designing an incremental dose counter for an inhaler comprising the steps of calculating nominal canister fire and

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dose counter positions for a dose counter actuator of the inhaler; calculating a failure/success rate for dose counters built to tolerance levels for counting each fire of inhalers in which the dose counter actuators may be applied; and selecting a tolerance level to result in said failure/success rate to be at or below/above a predetermined value. This is highly advantageous in that it allows an efficient and accurate prediction of the reliability of a series of inhaler counters made in accordance with the design.

The method of designing may include selecting the failure/success rate as a failure rate of no more than one in 50 million. The method of designing may include setting an average count position for dose counters built to the tolerances to be at or after an average fire position thereof during canister firing motion. The method of designing may include setting the average count position to be about 0.4 to 0.6 mm after the average fire position, such as about 0.48 mm after. The method of designing may include setting tolerances for the standard deviation of the fire position in dose counters built to the tolerances to be about 0.12 to 0.16 mm, such as about 0.141 mm. The method of designing may include setting tolerances for the standard deviation of the count positions in dose counters built to the tolerances to be about 0.07 to 0.09 mm, such as about 0.08 mm. A further aspect of the invention provides a computer implemented method of designing an incremental dose counter for an inhaler which includes the aforementioned method of designing.

A further aspect of the invention provides a method of manufacturing in a production run a series of incremental dose counters for inhalers which comprises manufacturing the series of dose counters in accordance with the aforementioned method of designing.

A further aspect of the invention provides a method of manufacturing a series of incremental dose counters for inhalers, which comprises manufacturing the dose counters with nominal canister fire and dose count positions of a dose counter actuator relative to a dose counter chassis (or inhaler main body), and which includes building the dose counters with the average dose count position in the series being, in canister fire process, at or after the average canister fire position in the series.

According to a further aspect of the invention, the method provides fitting each dose counter in the series of incremental dose counters to a corresponding main body of an inhaler.

These aspects advantageously provide for the production run of a series of inhalers and dose counters which count reliably in operation.

According to a further aspect of the invention, an incremental dose counter for a metered dose inhaler has a body arranged to retain a canister for movement of the canister relative thereto, the incremental dose counter having a main body, an actuator arranged to be driven and to drive an incremental output member in a count direction in response to canister motion, the actuator being configured to restrict motion of the output member in a direction opposite to the count direction. This advantageously enables an inhaler dose counter to keep a reliable count of remaining doses even if dropped or otherwise jolted.

The output member may comprise a ratchet wheel. The actuator may comprise a pawl and in which the ratchet wheel and pawl are arranged to permit only one-way ratcheting motion of the wheel relative to the pawl. The dose counter may include an anti-back drive member fixed to the main body. In a rest position of the dose counter, the ratchet wheel is capable of adopting a configuration in which a back surface of one tooth thereof engages the anti-back drive member and the pawl is spaced from an adjacent back

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surface of another tooth of the ratchet wheel without positive drive/blocking engagement between the pawl and wheel.

BRIEF DESCRIPTION OF THE DRAWINGS

The present invention may be carried out in various ways and preferred embodiment of a dose counter, inhaler and methods of assembly, design and manufacture will now be described with reference to the accompanying drawings in which:

FIG. 1 is an isometric view of a main body of an embodiment of an inhaler related to the invention together with a mouthpiece cap therefor;

FIG. 2 is a top plan view of the components as shown in FIG. 1;

FIG. 3A is a section on the plane 3A-3A in FIG. 2;

FIG. 3B is a view corresponding to FIG. 3A but with a dose counter fitted to the main body of the inhaler;

FIG. 4A is an exploded view of the inhaler main body, mouthpiece cap, dose counter and a dose counter window;

FIG. 4B is a view in the direction 4B in FIG. 4C of a spring retainer of the dose counter;

FIG. 4C is a top view of the spring retainer of FIG. 4B;

FIG. 5 is a bottom view of the assembled inhaler main body, mouthpiece cap, dose counter and dose counter window;

FIGS. 6A, 6B, 6C, 6D, 6E, 6F, 6G and 6H are various views of dose counter components of the inhaler;

FIGS. 7A and 7B are sectional views showing canister clearance inside the main body of the inhaler;

FIG. 7C is a further sectional view similar to that of FIG. 7B but with the canister removed;

FIG. 7D is a top plan view of the inhaler main body;

FIGS. 8A, 8B, 8C and 8D show the inhaler main body and dose counter components during assembly thereof;

FIG. 9 shows a sectional side view of a datum line for an actuator pawl of the dose counter;

FIGS. 10A, 10B, 10C, 10D, 10E and 10F show various side views of positions and configurations of the actuator pawl, a ratchet wheel, and a count pawl;

FIG. 11 shows distributions for tolerances of start, reset, fire, count and end positions for the actuator of the dose counter;

FIG. 12 is an enlarged version of part of FIG. 4A;

FIG. 13 shows an end portion of a tape of the dose counter;

FIG. 14 shows a computer system for designing the dose counter;

FIG. 15 is an isometric view of a stock bobbin modified in accordance with the present invention for use in the dose counter of the inhaler of FIGS. 1 to 14;

FIG. 16 shows an end view of the stock bobbin of FIG. 15;

FIG. 17 is a section through a longitudinal axis of the stock bobbin of FIGS. 15 and 16;

FIGS. 18A, 18B and 18C are views of the stock bobbin of FIGS. 15 to 17 mounted in the dose counter chassis of FIGS. 1 to 14, with the control elements of the forks of the second shaft (or split pin) having a profile slightly different to that in FIG. 6F, with the forks in a compressed configuration;

FIGS. 19A, 19B and 19C are views equivalent to FIGS. 18A to 18C but with the forks in a more expanded configuration due to a different rotational position of the stock bobbin;

FIG. 20 is an isometric view of the chassis assembled and including the stock bobbin of FIGS. 15 to 17 but excluding the tape for reasons of clarity;

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FIG. 21 is a view of a preferred embodiment of a dry powder inhaler in accordance with the present invention;

FIG. 22 is an exploded view of the inhaler of FIG. 21;

FIG. 23 is a view of a dose counter of the inhaler of FIG. 21;

FIG. 24 is an exploded view of the dose counter shown in FIG. 23;

FIG. 25 is an exploded view of parts of the inhaler of FIG. 21; and

FIG. 26 is a view of a yoke of the inhaler of FIG. 21.

DETAILED DESCRIPTION OF THE INVENTION

FIG. 1 shows a main body 10 of a manually operated metered dose inhaler 12 in accordance with an embodiment related to the present invention and having a mouthpiece cap 14 securable over a mouthpiece 16 of the main body.

The main body has a canister chamber 18 into which a canister 20 (FIG. 7A) is slideable. The canister 20 has a generally cylindrical main side wall 24, joined by a tapered section 26 to a head portion 28 having a substantially flat lower face 30 which has an outer annular drive surface 32 arranged to engage upon and drive an actuation pin 34 of a dose counter 36 as will be described. Extending centrally and axially from the lower face 30 is a valve stem 38 which is arranged to sealingly engage in a valve stem block 40 of the main body 10 of the inhaler 12. The valve stem block 40 has a passageway 42 leading to a nozzle 44 for directing the contents of the canister 20, namely active drug and propellant, towards an air outlet 46 of the inhaler main body 12. It will be appreciated that due to gaps 48 between the canister 20 and an inner wall 50 of the main body 10 of the inhaler 12 an open top 52 of the main body 10 forms an air inlet into the inhaler 12 communicating via air passageway 54 with the air outlet 46, such that canister contents exiting nozzle 44 mix with air being sucked by the user through the air passageway 54 in order to pass together through the air outlet and into the mouth of the user (not shown).

The dose counter 36 will now be described. The dose counter 36 includes an actuation pin 34 biased upwardly from underneath by a return spring 56 once installed in the main body 10. As best shown in FIGS. 4A, 6H and 8A, the pin 34 has side surfaces 58, 60 arranged to slide between corresponding guide surfaces 62, 64 located in a dose counter chamber 66 of the main body 10, as well as an end stop surface 68 arranged to engage a corresponding end stop 70 formed in the dose counter chamber 66 to limit upward movement of the pin 34. The pin 34 has a top part 72 which is circularly cylindrical and extends through an aperture 74 formed through a separator wall 76 which separates the canister chamber 18 from the dose counter chamber 66. The top part 72 of the pin 34 has a flat top surface 78 which is arranged to engage the outer annular drive surface 32 of the canister 20.

The actuation pin 34 is integrally formed with a drive or actuator pawl 80. The actuator pawl 80 has a generally inverted U-shape configuration, having two mutually spaced and parallel arms 82, 84 extending from a base portion of the actuation pin 34, each holding at respective distal ends 88 thereof opposite ends of a pawl tooth member 90 which extends in a direction substantially perpendicular to the arms 82, 84, so as to provide what may be considered a "saddle" drive for pulling on each of the 11 drive teeth 92 of a ratchet wheel 94 of an incremental drive system 96 or ratchet mechanism 96 of the dose counter 36. As shown for example in FIG. 10B, the pawl tooth member 90 has a sharp lower

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longitudinal side edge 98 arranged to engage the drive teeth 92, the edge-to-surface contact provided by this engagement providing very accurate positioning of the actuator pawl 80 and resultant rotational positioning of the ratchet wheel 94.

The dose counter 36 also has a chassis preassembly 100 which, as shown in FIGS. 4A and 6A, includes a chassis 102 having a first shaft 104 receiving the ratchet wheel 94 which is secured to a tape reel shaft 106, and a second shaft (or split pin) 108 which is parallel to and spaced from the first shaft 104 and which slidably and rotationally receives a tape stock bobbin 110.

As shown in FIG. 6B, when the inhaler has not been used at all, the majority of a tape 112 is wound on the tape stock bobbin 110 and the tape 112 has a series of regularly spaced numbers 114 displayed therealong to indicate a number of remaining doses in the canister 20. As the inhaler is repeatedly used, the ratchet wheel 94 is rotated by the actuator pawl 80 due to operation of the actuation pin 34 by the canister 20 and the tape 112 is incrementally and gradually wound on to the tape reel shaft 106 from the second shaft 108. The tape 112 passes around a tape guide 116 of the chassis 102 enabling the numbers 114 to be displayed via a window 118 in a dose counter chamber cover 120 having a dose marker 132 formed or otherwise located thereon.

As shown in FIGS. 6A and 6D, the second shaft 108 is forked with two forks 124, 126. The forks 124, 126 are biased away from one another. The forks have located thereon at diametrically opposed positions on the second shaft 108 friction or control elements 128, 130, one on each fork. Each control element extends longitudinally along its respective fork 124, 126 and has a longitudinally extending friction surface 132, 134 which extends substantially parallel to a longitudinal axis of the second shaft and is adapted to engage inside a substantially cylindrical bore 136 inside the tape stock bobbin 110. This control arrangement provided between the bore 136 and the control elements 128, 130 provides good rotational control for the tape stock bobbin 110 such that it does not unwind undesirably such as when the inhaler is dropped. The tape force required to unwind the tape stock bobbin 110 and overcome this friction force is approximately 0.1 N.

As can be seen in FIG. 6D, as well as FIGS. 6G and 10A to 10F, the chassis 102 is provided with an anti-back drive tooth 138 or count pawl 138 which is resiliently and substantially fixedly mounted thereto. As will be described below and as can be seen in FIGS. 10A to 10F, when the actuation pin 34 is depressed fully so as to fire the metered valve (not shown) inside the canister 20, the actuator pawl 80 pulls down on one of the teeth 92 of the ratchet wheel 94 and rotates the wheel 94 anticlockwise as shown in FIG. 6D so as to jump one tooth 92 past the count pawl 138, thereby winding the tape 112 a distance incrementally relative to the dose marker 122 on the dose counter chamber 120 so as to indicate that one dose has been used.

With reference to FIG. 10B, the teeth of the ratchet wheel 94 have tips 143 which are radiused with a 0.1 mm radius between the flat surfaces 140, 142. The ratchet wheel 94 has a central axis 145 which is 0.11 mm above datum plane 220 (FIG. 9). A top/nose surface 147 of the anti-back drive tooth 138 is located 0.36 mm above the datum plane 220. The distance vertically (i.e. transverse to datum plane 220—FIG. 9) between the top nose surface 147 of the anti-back drive tooth is 0.25 mm from the central axis 145 of the wheel 94. Bump surface 144 has a lateral extent of 0.20 mm, with a vertical length of a flat 145' thereof being 1 mm, the width of the bump surface being 1.22 mm (in the direction of the axis 145), the top 149 of the bump surface 144 being 3.02

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mm vertically below the axis 145, and the flat 145' being spaced a distance sideways (i.e. parallel to the datum plane 220) 2.48 mm from the axis 145. The top surface 78 of the pin 34 (FIG. 6H) is 11.20 mm above the datum plane 220 (FIG. 9) when the actuator pawl 80 and pin 34 are in the start configuration. The length of the valve stem 22 is 11.39 mm and the drive surface 32 of the canister 20 is 11.39 mm above the datum plane 220 when the canister is at rest waiting to be actuated, such that there is a clearance of 0.19 mm between the canister 20 and the pin 34 in this configuration.

FIGS. 10A and 10B show the actuator pawl 80 and ratchet wheel 94 and count pawl 138 in a start position in which the flat top 78 of the pin 34 has not yet been engaged by the outer annular drive surface 32 of the canister 20 or at least has not been pushed down during a canister depression.

In this "start" position, the count pawl 138 engages on a non-return back surface 140 of one of the teeth 92 of the ratchet wheel 94. The lower side edge 98 of the actuator pawl is a distance "D" (FIG. 9) 1.33 mm above datum plane 220 which passes through bottom surface or shoulder 41 of valve stem block 40, the datum plane 220 being perpendicular to a main axis "X" of the main body 10 of the inhaler 12 which is coaxial with the centre of the valve stem block bore 43 and parallel to a direction of sliding of the canister 20 in the main body 10 of the inhaler 12 when the canister is fired.

As shown in FIG. 10B, an advantageous feature of the construction is that the pawl tooth/actuator 90 acts as a supplementary anti-back drive member when the inhaler 12 is not being used for inhalation. In particular, if the inhaler 12 is accidentally dropped, resulting in a jolt to the dose counter 36 then, if the wheel 94 would try to rotate clockwise (backwards) as shown in FIG. 10B, the back surface 140 of a tooth will engage and be blocked by the tooth member 90 of the pawl 80. Therefore, even if the anti-back drive tooth 138 is temporarily bent or overcome by such a jolt, undesirable backwards rotation of the wheel 94 is prevented and, upon the next canister firing sequence, the pawl 90 will force the wheel 94 to catch up to its correct position so that the dose counter 36 continues to provide correct dosage indication.

FIG. 10C shows a configuration in which the actuator pawl 80 has been depressed with the pin 34 by the canister 20 to a position in which the side edge 98 of the pawl tooth member 90 is just engaged with one of the teeth 92 and will therefore upon any further depression of the pin 34 begin to rotate the wheel 94. This is referred to as a "Reset" position or configuration. In this configuration, the lower side edge 98 of the actuator 80 is 0.64 mm above the datum plane 220.

FIG. 10D shows a configuration in which the actuator pawl 80 has been moved to a position lower than that shown in FIG. 10C and in which the metered dose valve (not shown) inside the canister has at this very position fired in order to eject active drug and propellant through the nozzle 44. It will be noted that in this configuration the count pawl 138 is very slightly spaced from the back surface 140 of the same tooth 92 that it was engaging in the configuration of FIG. 10D. The configuration shown in FIG. 10D is known as a "Fire" configuration. In this configuration the lower side edge 98 of the actuator 80 is 0.47 mm below the datum plane 220.

FIG. 10E shows a further step in the sequence, called a "Count" position in which the actuator pawl 80 has rotated the ratchet wheel 94 by the distance circumferentially angularly between two of the teeth 92, such that the count pawl 138 has just finished riding along a forward surface 142 of one of the teeth 92 and has resiliently jumped over the tooth

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into engagement with the back surface **140** of the next tooth. Accordingly, in this "Count" configuration, a sufficiently long stroke movement of the pin **34** has occurred that the tape **112** of the dose counter **36** will just have counted down one dose. In this configuration, the lower side edge **98** of the actuator is 0.95 mm below the datum plane **220**. Accordingly, in this position, the actuator **80** generally, including edge **98**, is 0.48 mm lower than in the fire configuration. It has been found that, although the count configuration happens further on than the fire configuration, counting is highly reliable, with less than 50 failed counts per million. This is at least partially due to momentum effects and to the canister releasing some back pressure on the user in some embodiments as its internal metering valve fires.

In the configuration of FIG. **10F**, the pawl **80** has been further depressed with the pin **34** by the canister **20** to a position in which it is just disengaging from one of the teeth **92** and the actuator pawl **80** is assisted in this disengagement by engagement of one of the arms **84** with a bump surface **144** on the chassis **102** (see FIG. **6G**) and it will be seen at this point of disengagement, which is called an "End" configuration, the count pawl **138** is positioned exactly halfway or substantially halfway between two of the drive teeth **92**. This advantageously means therefore that there is a minimum chance of any double counting or non-counting, which would be undesirable. In the end configuration, the side edge **98** of the actuator is 1.65 mm below the datum plane **220**. It will be appreciated that any further depression of the actuator pawl **80** and pin **34** past the "End" configuration shown in FIG. **10F** will have no effect on the position of the tape **112** displayed by the dose counter **36** since the actuator pawl **80** is disengaged from the ratchet wheel **94** when it is below the position shown in FIG. **10F**.

As shown in FIGS. **7C** and **7D**, the inner wall **50** of the main body **10** is provided with a two-step support rail **144** which extends longitudinally along inside the main body and is located directly adjacent the aperture **74**. As shown in FIG. **7B** a diametrically opposed two-step support rail **146** is also provided and this diametrically opposed in the sense that a vertical plane (not shown) can pass substantially directly through the first rail **144**, the aperture **74**, a central aperture **148** of the valve stem block **40** (in which canister stem **25** is located) and the second two-step support rail **146**. As shown in FIG. **7A** and schematically in FIG. **7B**, the rails **144**, **146** provide a maximum clearance between the canister **20** and the rails **144**, **146** in a radial direction of almost exactly 0.3 mm, about 0.25 to 0.35 mm being a typical range. This clearance in this plane means that the canister **20** can only rock backwards and forwards in this plane towards away from the actuation pin **34**. A relatively small distance and this therefore prevents the canister wobbling and changing the height of the actuation pin **34** as to undesirably alter the accuracy of the dose counter **36**. This is therefore highly advantageous.

The inner wall **50** of the main body **10** is provided with two further two-step rails **150** as well as two pairs **152**, **154** of rails extending different constant radial amounts inwardly from the inner wall **50**, so as to generally achieve a maximum clearance of almost exactly 0.3 mm around the canister **20** for all of the rails **PH**, **146**, **150**, **152**, **154** spaced around the periphery of the inner wall **50**, in order to prevent undue rocking while still allowing canister motion freely inside the inhaler **12**. It will be clear from FIG. **7C** for example that the two-step rails have a first portion near an outlet end **156** of the canister chamber **18**, the first portion having a substantially constant radial or inwardly-extending width, a first step **160** leading to a second portion **162** of the rail, the

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second portion **102** having a lesser radial or inwardly extending extent than the first portion **156**, and finally a second step **164** at which the rail merges into the main inner wall **50** main surface.

A method of assembling the inhaler **12** will now be described.

With reference to FIG. **8A**, the main body **10** of the inhaler **12** is formed by two or more plastics mouldings which have been joined together to the configuration shown.

As shown in FIG. **8B**, the actuator pawl **80** and pin **34** are translated forward into position into a pin receiving area **166** in the dose counter chamber **66** and the pin **34** and actuator **80** may then be raised until the pin **34** emerges through the aperture **74**.

Next, the return spring **56** may be inserted below the pin **34** and a generally cylindrical annular lower end **168** of the spring **56** may be moved by a tweezer or tweezer-like assembly tool (not shown) into engagement with a shelf **170** of a spring retainer **172** in the dose counter chamber **66**. The spring retainer **172** is U-shaped and the shelf **170** is U-shaped and has a recess **174** formed below it. As shown in FIGS. **4B**, **4C** and **12** shelf **170** includes three chamfer surfaces **176**, **178**, **180** arranged to assist in moving the lower end of the spring **168** into position onto the shelf using the assembly tool (not shown). Once the lower end of the spring **168** is in place, the assembly tool (not shown) can easily be removed at least partly via the recess **174** below the lower end **168** of the spring **56**.

The tape **112** is attached at one end (not shown) to the tape stock bobbin **110** and is wound onto the bobbin by a motor **200** (FIG. **13**) having a hexagonal output shaft **202** which engages in a hexagonal socket **204** (FIG. **6B**) of the bobbin. During winding, the tape is monitored by a sensor **206**, which may be in the form of a camera or laser scanner, which feeds data to a computer controller **205** for the motor **200**. The controller **205** recognises three positioning markers **210** in the form of lines across the tape **112** and stops the motor **202** when the tape **112** is nearly fully wound onto the bobbin **110**, such that the distal end **212** of the tape **112** can be secured, e.g. by adhesive, to the tape reel shaft **106**. The controller **205** also recognises a pixelated tape size marker **214** observed by the sensor **206** and logs in a stocking system data store **217** details of the tape **112** such as the number of numbers **114** on the tape, such as one hundred and twenty or two hundred numbers **114**. Next, the tape reel shaft is wound until an appropriate position of the lines **210** at which a priming dot **216** will, once the bobbin **110** and reel shaft **106** are slid onto the second shaft **108** and second shaft **104**, be in a position to be located in the window **118** when the inhaler **12** is fully assembled. In the embodiments, the bobbin **110** and reel shaft **106** may be slid onto the shafts **108**, **104** before the tape **112** is secured to the reel shaft **106** and the reel shaft may then be wound to position the priming dot **216**.

Next, the assembled dose counter components of the chassis preassembly **100** shown in FIG. **6B** may as shown in FIG. **8C** be inserted into the dose counter chamber **66**, with pins **182**, **184**, **186** formed on the main body **10** in the dose counter chamber **66** passing through apertures or slots **188**, **190**, **192** formed on the chassis **102**, such that the pins **182**, **184**, **186** extend through (or at least into) the apertures or slots **188**, **190**, **192**. With the chassis **102** being relatively firmly pushed towards the main body **10**, the pins **182**, **184**, **186** are then heat staked and the chassis **102** is therefore after this held very firmly in position in the main body and is unable to move, thereby assisting in providing great accuracy for the dose counter **36**. Next, as shown in FIG. **8D**, the

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dose counter chamber cover **120** may be fitted over the dose counter chamber **66** and may be secured in place such as by welding, with the priming dot **216** being displayed through the window.

The user can, when readying the inhaler **12** for first use, prime the inhaler by depressing the canister **20** three times which will bring the first number **114** on the tape into display through the window **118** in place of the priming dot **216**, the number **114** shown in FIG. **8D** being “200”, thereby indicating that 200 doses are remaining to be dispensed from the canister **20** and inhaler **12**.

As shown in FIG. **8D**, and in FIG. **5**, an open drain hole **194** is provided at the bottom of the dose counter chamber **66** by a substantially semi-circular cut-out or recess formation **196** in a lower surface **198** of the main body **10** of the inhaler. Accordingly, if the user (not shown) should decide to wash the main body **10** of the inhaler, for example after encountering an unhygienic situation or simply as a matter of choice, the drain hole **194** allows initial draining of water from inside the dose counter chamber **66** and also thereafter evaporation of water or any aqueous matter in the dose counter chamber **66** so that the window **118** does not mist up undesirably.

FIG. **14** shows a computer system **230** for designing the dose counter **36** and in particular for calculating distributions representative of average positions and standard deviations in a production series of inhalers of the start, reset, fire, count and end positions of the actuator lower side edge **98** relative to the datum plane **220** (FIG. **9**) and therefore of the actuator pawl **80** generally relative to the ratchet wheel **94**, chassis **102** and, when the inhaler **12** is fully assembled, the main body **10** of the inhaler **12**. The computer system **230** includes a data store **232**, a CPU **234**, an input device **236** (such as a keyboard or communication port) and an output device **238** (such as a communications port, display screen and/or printer). A user may enter data via the input device **236** which may be used by the CPU **234** in a mathematical calculation to predict count failure rates when the various dose counters are to be built in a series with dose counter positions set with given averages and standard deviations and taking into account any momentum/inertia effects and metering valve user-back-pressure reduction effect which will occur upon canister firing of a given type of canister. The computer system **230** is thus mathematically used to design the distributions. For the inhaler **12** described herein with the dose counter **36** and canister **20**, the distributions are designed as shown in FIG. **11**. The x axis shows distance of the lower side surface **98** of the actuator **80** above the datum plane **220** and the y axis is representative of the distribution. Thus, curve **240** shows that the start configuration has an average 1.33 mm above the datum plane **200** (standard deviation is 0.1 mm), curve **242** shows that the reset configuration has an average of 0.64 mm above the datum plane **220** (standard deviation is 0.082 mm), curve **244** shows the fire configuration has an average 0.47 mm below the datum plane **220** (standard deviation is 0.141 mm), curve **246** shows the count configuration has an average 0.95 mm below the datum plane **220** (standard deviation is 0.080 mm), and curve **248** shows the end configuration has an average of 1.65 mm below the datum plane **220** (standard deviation is 0.144 mm).

FIGS. **15** to **20** show a version of the inhaler modified in accordance with the present invention. In these drawings, the same reference numerals have been used to those in the earlier drawings to denote the equivalent components. The inhaler **12** is the same as that in FIGS. **1** to **14** apart from the following modifications.

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First, it can be seen that there is a modification in that the drive teeth **92** of the ratchet wheel **94** have a different profile to that in FIGS. **1** to **14**. There are also only nine ratchet teeth **94** in this embodiment instead of eleven.

Additionally, as shown in FIGS. **18C** and **19C**, the control elements **128**, **130** on the forks **124**, **126** of the second shaft **108** have a tapered profile which is different to the profile of the control elements **128**, **130** shown in FIG. **6F**. Either profile can be used in the embodiment of FIGS. **15** to **20** however.

Furthermore, as shown in FIG. **15**, the tape stock bobbin **110** has an inwardly facing generally cylindrical engagement surface **300** with a wavelike form extending partially therealong. The engagement surface **300** has a cross-section **301** perpendicular to the longitudinal length of the stock bobbin **110** which is constant therealong. This cross-section **301** can be seen in FIG. **16** and consists of a series of ten regularly spaced concavities **302** and ten convex wall portions **304**. The convex wall portions **304** are equi-spaced between the concavities **302**. Each concavity **302** has a radius of 0.2 mm. Each convex wall portion **304** also has a radius of 0.2 mm. Finally, the cross section **301** also includes flat wall portions **306** between all of the radiused wall portions of the concavities **302** and convex wall portions **304**. The geometry of the cross-section **301** is therefore defined by the radii of the concavities **302** and convex wall portions **304**, the flat wall portions **306** and the fact that there are ten concavities **302** and convex wall portions **304**.

The minor diameter of the engagement surface **300**, i.e. between the tips of opposite convex wall portions **304**, is 2.46 mm. The major diameter of the engagement surface **300**, i.e. between the outermost portions of the concavities **302**, is 2.70 mm. The undeformed tip to tip maximum diameter of the forks **124**, **126** of the split pin (the second shaft) **108**, i.e. in the region of the maximum radio extent of the control elements **128**, **130**, is 3.1 millimetres and it will therefore be appreciated that the forks **124**, **126** are resiliently compressed once the stock bobbin **110** has been assembled onto the split pin **108** in all rotational configurations of the stock bobbin **110** relative to the split pin **108**. The minimum gap between the forks **124**, **126** in the plane of the cross sections of FIGS. **18C** and **19C** is 1 mm when the split pin **108** is in the undeformed, pre-inserted state. When the split pin **108** is at maximum compression, as shown in FIGS. **18A** to **18C** when the control elements **128**, **130** are shown to be engaged on top of the convex wall portions **304**, the gap **308** between the tips **310**, **312** of the forks **124**, **126** is 0.36 mm. On the other hand, when the split pin **108** is at minimum compression (once inserted into the stock bobbin) as shown in FIGS. **19A** to **19C**, when the control elements **128**, **130** rest in the concavities **302**, the gap between the tips **310**, **312** of the forks **124**, **126** is 0.6 mm. The control elements **128**, **130** are outwardly radiused with a radius also of 0.2 mm such that they can just rest on the concavities **302** with full surface contact (at least at an axial location on the split pin where the tapered control elements are at their maximum radial extent), without rattling in, locking onto or failing to fit in the concavities **302**. The radii of the control elements **128**, **130** is therefore preferably substantially the same as the radii of the concavities **302**.

It will be appreciated that whereas FIGS. **18B** and **19B** are end views along the coaxial axis of the stock bobbin **110** and split pin **108**, FIGS. **18A** and **19A** are cross-sections. FIG. **19A** is a section on the plane A-A' in FIG. **19C** and FIG. **18A** is a section at the same plane, but of course with the stock bobbin **110** rotated relative to the split pin **108**.

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As the inhaler 12 is used and the ratchet wheel 94 rotates in order to count used doses, the stock bobbin rotates incrementally through rotational positions in which rotation is resisted, i.e. due to increasing compression of the split pin 108 at such rotational positions, and rotational positions in which rotation is promoted, i.e. due to decreasing compression of the split pin 108 at such rotational positions and this may involve a click forward of the stock bobbin 110 to the next position equivalent to that in FIGS. 19A to 19C in which the control elements 128, 130 of the split pin art located in the concavities 302. This functionality firstly allows the stock bobbin to unwind during use as required, but also prevents the tape 112 from loosening during transit if the inhaler 12 is dropped, such as onto a hard surface. This is highly advantageous, since the tape 11 is prevented from moving to a position in which it will give an incorrect reading regarding the number of doses in the canister.

During compression and expansion of the forks in the radial direction between the two configurations shown in FIGS. 18C and 19C, the forks 124, 126 rotate about a point 316 on the split pin where the forks 124, 126 come together. This rotational action means that there is a camming action between the forks 124, 126 and the engagement surface 300 without significant friction but, nevertheless, the resilient forces provided by the regulator formed by the engagement surface 300 and forks 124, 126 are able to regulate unwinding of the tape such that it does not easily occur during transit or if the inhaler 12 is dropped. It has been found during testing that a force of 0.3 to 0.4 N needs to be applied to the tape 112 to overcome the regulator at the stock bobbin 110. 0.32 N is achieved with the control elements 128 having the profile shown in FIG. 19C and 0.38 N is achieved with the profile of the control elements 128 altered to be as shown as described with reference to FIG. 6F. These forces are substantially higher than the 0.1 N force mentioned above and undesirable movement of the tape is substantially avoided even if the inhaler is dropped onto a hard surface. The modified arrangement of FIGS. 15 to 20 does not provide this force "constantly" such that there is overall not an undesirably high friction of the tape 112 as it passes over the other components of the dose counter because, due to the incremental nature of the resilient forces at the regulator, the tape 112 can incrementally relax as it slides over the stationary chassis components.

Instead of having ten concavities 302 and convex wall portions 304, other numbers may be used, such as 8 or 12. However, it is preferred to have an even number, especially since two control elements 128, 130 are provided, so that all of the control elements 128, 130 will expand and contract simultaneously. However, other arrangements are envisaged with 3 or more forks and the number of concavities/convex wall portions may be maintained as an integer divisible by the number of forks to maintain a system with simultaneous expansion/contraction. For example, the use of 9, 12 or 15 concavities/convex wall portions with 3 forks is envisaged.

Instead of having the engagement surface 300 on the inside of the stock bobbin 110, it could be placed on the outside of the stock bobbin 110 so as to be engaged by flexible external legs/pawls or similar.

It will be noted that the regulator provided by the engagement surface 300 and forks 124, 126 does not only allow rotation of the stock bobbin in one direction as is the case with the ratchet wheel 94. Rotation in both directions is possible, i.e. forwards and backwards. This means that during assembly, the stock bobbin 110 can be wound backwards during or after fitting the bobbin 100, shaft 106 and tape 112 onto the carriage 102, if desired.

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The stock bobbin 110 and the carriage 102 including the split pin 108 are both moulded of polypropylene material.

It will be seen from FIG. 16 that the cross-sectional shape 301 is not symmetrical within the hexagonal socket 204. This has enabled the hexagonal socket 204 to be maintained at a useful size while still allowing the desired size and geometry of the cross section 301 to fit without interfering with the hexagonal shape of the hexagonal socket 204 and also permits moulding to work during manufacture.

As shown in FIG. 17, the stock bobbin 110 has a series of four circumferential ribs 330 inside it and a spaced therealong. These hold the stock bobbin 110 on the correct side of the mould tool during moulding.

FIGS. 21 and 22 show a preferred embodiment in accordance with the invention of an inhaler 510 for dispensing a dry-powdered medicament in metered doses for patient inhalation. The inhaler 510 is as disclosed in FIGS. 1 to 16 or EP-A-1330280, the contents of which are hereby fully incorporated herein by reference, but with the stock bobbin 110 and second shaft 108 of the dose counter 516 modified so as to be as in FIGS. 15 to 20 hereof. Thus, the dry powder inhaler 510 generally includes a housing 518, and an assembly 512 received in the housing (see FIG. 21). The housing 518 includes a case 520 having an open end 522 and a mouthpiece 524 (FIG. 25) for patient inhalation, a cap 526 secured to and closing the open end 522 of the case 520, and a cover 528 pivotally mounted to the case 520 for covering the mouthpiece 524. As shown in FIG. 22, the inhaler 510 also includes an actuation spring 569, first yoke 566 with opening 572, bellows 540 with crown 574, a reservoir 514, second yoke 568 with hopper 542 and dose counter 516 mounted thereto, and case 520 has transparent window 5130 thereon for viewing dose counter tape indicia 5128. The dose metering system also includes two cams 570 mounted on the mouthpiece cover 528 and movable with the cover 528 between open and closed positions. The cams 570 each include an opening 580 for allowing outwardly extending hinges 582 of the case 520 to pass therethrough and be received in first recesses 584 of the cover 528. The cams 570 also include bosses 586 extending outwardly and received in second recesses 588 of the cover 528, such that the cover 528 pivots about the hinges 582 and the cams 570 move with the cover 528 about the hinges 582. As described in EP-A-1330280, cams 570 act upon cam followers 578 to move second yoke 568 up and down and thereby operate dose counter by engagement of pawl 5138 on the second yoke 568 with teeth 5136. Remaining components of the inhaler are provided as, and operate as described, in EP-A-1330280.

The dose counting system 516 therefore includes a ribbon or tape 5128 (FIGS. 23 & 24), having successive numbers or other suitable indicia printed thereon, in alignment with a transparent window 5130 provided in the housing 18 (see FIG. 22). The dose counting system 516 includes the rotatable stock bobbin 110 (as described above), an indexing spool 5134 rotatable in a single direction, and the ribbon 5128 rolled and received on the bobbin 110 and having a first end 5127 secured to the spool 5134, wherein the ribbon 5128 unrolls from the bobbin 110 so that the indicia are successively displayed as the spool 5134 is rotated or advanced. In FIGS. 23 and 24 the wavelike engagement surface 300 of the bobbin 110 is not shown for the purposes of clarity.

The spool 134 is arranged to rotate upon movement of the yokes 566, 568 to effect delivery of a dose of medicament from reservoir 514, such that the number on the ribbon 5128 is advanced to indicate that another dose has been dispensed by the inhaler 510. The ribbon 5128 can be arranged such that the numbers, or other suitable indicia, increase or

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decrease upon rotation of the spool **5134**. For example, the ribbon **5128** can be arranged such that the numbers, or other suitable indicia, decrease upon rotation of the spool **5134** to indicate the number of doses remaining in the inhaler **510**. Alternatively, the ribbon **5128** can be arranged such that the numbers, or other suitable indicia, increase upon rotation of the spool **5134** to indicate the number of doses dispensed by the inhaler **10**.

The indexing spool **5134** includes radially extending teeth **5136**, which are engaged by pawl **5138** extending from a cam follower **578** of the second yoke **568** upon movement of the yoke to rotate, or advance, the indexing spool **5134**. More particularly, the pawl **5138** is shaped and arranged such that it engages the teeth **5136** and advances the indexing spool **5134** only upon the mouthpiece cover **528** being closed and the yokes **566**, **568** moved back towards the cap **526** of the housing **518**.

The dose counting system **516** also includes a chassis **5140** that secures the dose counting system to the hopper **542** and includes shafts **108**, **5144** for receiving the bobbin **110** and the indexing spool **5134**. As described above with reference to FIGS. **1** to **20**, the bobbin shaft **108** is forked and includes radially nubs **5146** for creating a resilient resistance to rotation of the bobbin **110** on the shaft **108** by engaging with the wavelike engagement surface **300** inside the bobbin **110**. A clutch spring **5148** is received on the end of the indexing spool **5134** and locked to the chassis **5140** to allow rotation of the spool **5134** in only a single direction.

Various modifications may be made to the embodiment shown without departing from the scope of the invention as defined by the accompanying claims as interpreted under patent law.

What is claimed is:

1. An incremental dose counter for a metered dose inhaler having a body arranged to retain a canister for movement of the canister relative thereto, the incremental dose counter having a main body, an actuator arranged to be driven and

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to drive an incremental output member in a count direction in response to canister motion, the actuator being configured to restrict motion of the output member in a direction opposite to the count direction, such that the actuator acts as an anti-back drive member when the actuator is in a non-depressed position, and wherein the incremental dose counter further comprises a second anti-back member configured to restrict motion of the output member in a direction opposite to the count direction when the actuator is disengaged from the output member by a bump surface.

2. The incremental dose counter as claimed in claim **1** in which the output member comprises a ratchet wheel.

3. The incremental dose counter as claimed in claim **2** in which the actuator comprises a pawl and in which the ratchet wheel and pawl are arranged to permit only one way ratcheting motion of the ratchet wheel relative to the pawl.

4. The incremental dose counter as claimed in claim **3** wherein the second anti-back member is fixed to the main body.

5. The incremental dose counter as claimed in claim **4** in which, when in a rest position of the dose counter, the ratchet wheel is capable of adopting a configuration in which a back surface of one tooth thereof engages the second anti-back member and the pawl is spaced from an adjacent back surface of another tooth of the ratchet wheel without positive drive/blocking engagement between the pawl and ratchet wheel.

6. A dose counter as claimed in claim **1** wherein an incremental counting system is arranged to move a counter display incrementally in a first direction from a first station to a second station in response to actuation input, wherein a regulator is provided which is arranged to act upon the counter display at the first station to regulate motion of the counter display at the first station to incremental movements.

* * * * *

EXHIBIT K

(12) **United States Patent**
Buck et al.

(10) **Patent No.: US 11,559,637 B2**

(45) **Date of Patent: Jan. 24, 2023**

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15/0091; A61M 15/08; A61M 2205/18;
A61M 2210/06; A61M 2210/0625;
(Continued)

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Paul Prendergast, County Carlow (IE);
Declan Walsh, County Kilkenny (IE)

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(*) Notice: Subject to any disclaimer, the term of this
patent is extended or adjusted under 35
U.S.C. 154(b) by 541 days.

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Primary Examiner — Justine R Yu

Assistant Examiner — Matthew D Ziegler

(51) **Int. Cl.**

A61M 15/00 (2006.01)

A61M 15/08 (2006.01)

(74) *Attorney, Agent, or Firm* — Morgan, Lewis &
Bockius LLP

(Continued)

(52) **U.S. Cl.**

CPC **A61M 15/0025** (2014.02); **A61K 9/007**
(2013.01); **A61K 31/439** (2013.01);

(Continued)

(58) **Field of Classification Search**

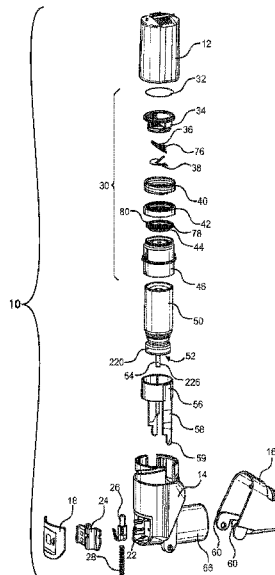
CPC A61K 9/007-008; A61K 31/439; A61K
31/569; A61M 15/0021; A61M 15/0025;
A61M 15/0026; A61M 15/0066; A61M
15/0068; A61M 15/007; A61M 15/0071;

(57)

ABSTRACT

An inhaler (10) has a main body for accommodating a
medicament reservoir (84), a canister fire system for moving
a canister (50) to release a dose in response to air flow, a cap
housing (12) for enclosing the canister fire system and
canister within an interior chamber defined by the main body
(14) and a cap housing, wherein a lock system (250) is
provided for locking the cap housing on the main body.

50 Claims, 21 Drawing Sheets



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- (52) **U.S. Cl.**
CPC *A61K 31/569* (2013.01); *A61M 15/009* (2013.01); *A61M 15/0021* (2014.02); *A61M 15/0066* (2014.02); *A61M 15/0071* (2014.02); *A61M 15/0091* (2013.01); *A61M 15/08* (2013.01); *A61P 11/00* (2018.01); *A61P 11/06* (2018.01); *B65D 41/0414* (2013.01); *B65D 41/0428* (2013.01); *B65D 55/16* (2013.01); *A61M 15/0026* (2014.02); *A61M 15/0076* (2014.02); *A61M 2205/18* (2013.01)
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- (58) **Field of Classification Search**
CPC .. A61P 11/00; A61P 11/06; B65D 41/02-086; B65D 55/16
See application file for complete search history.
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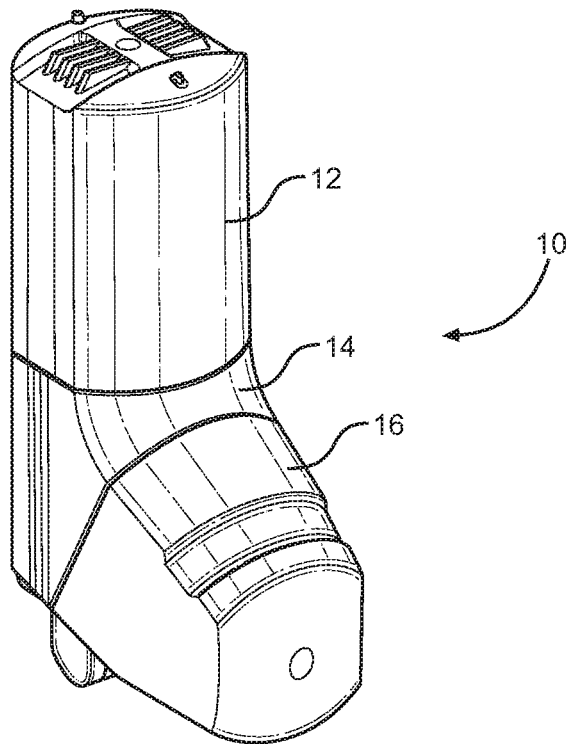


FIG. 1A

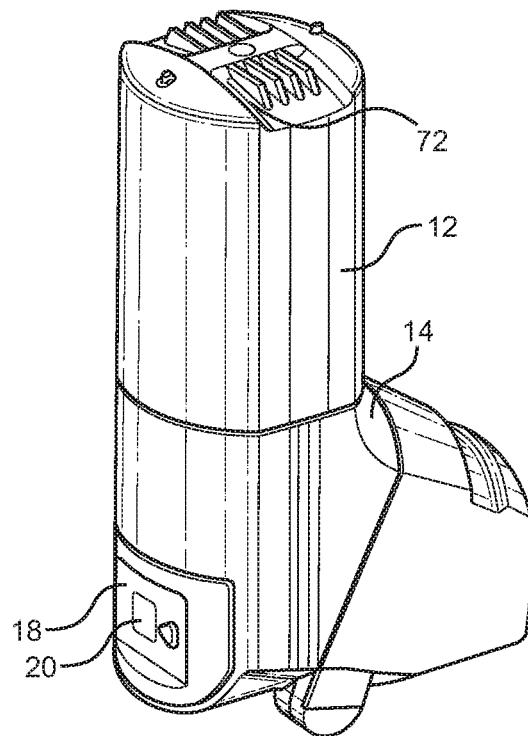
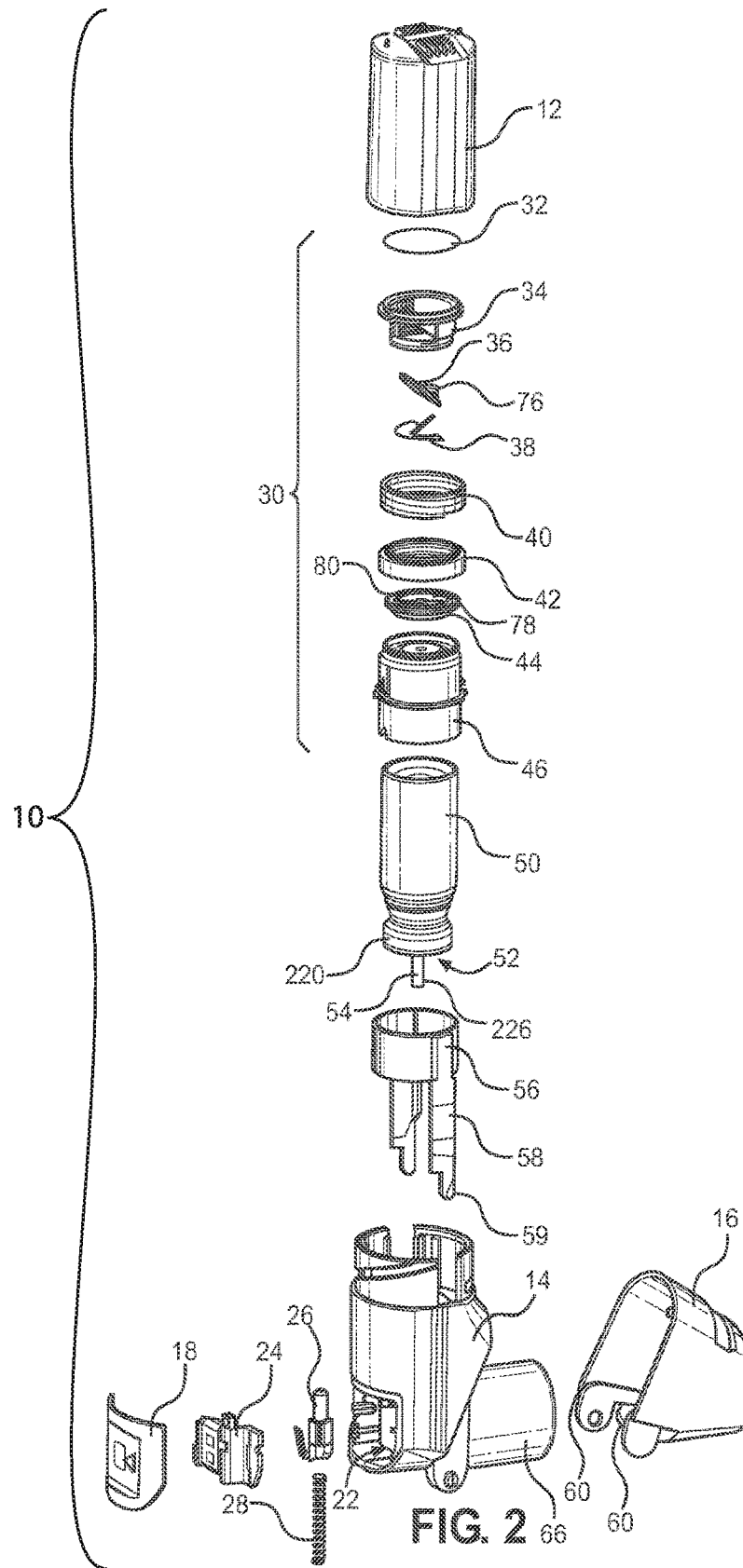


FIG. 1B



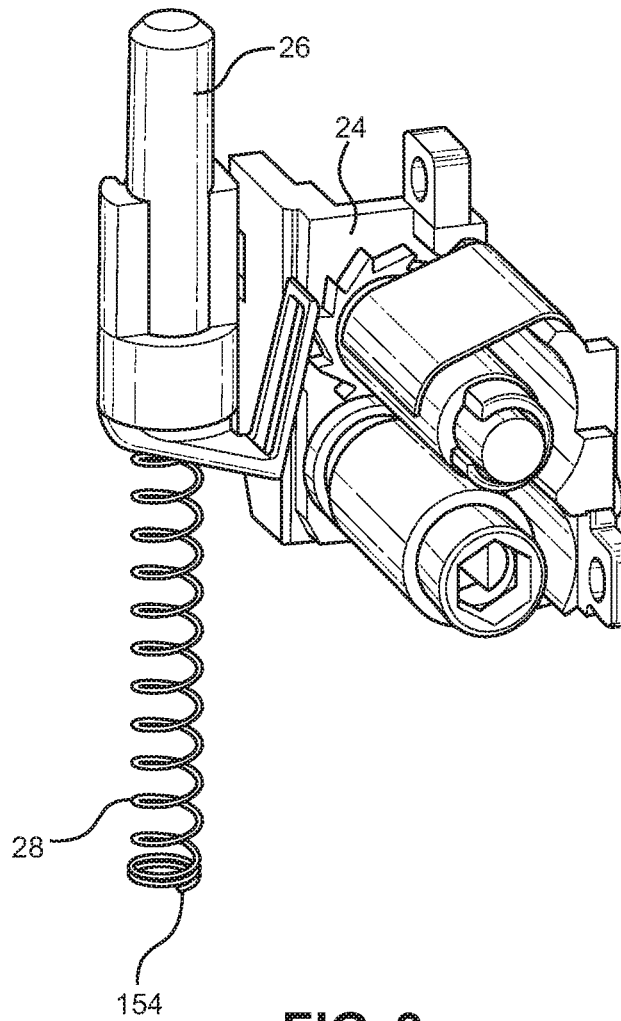


FIG. 3

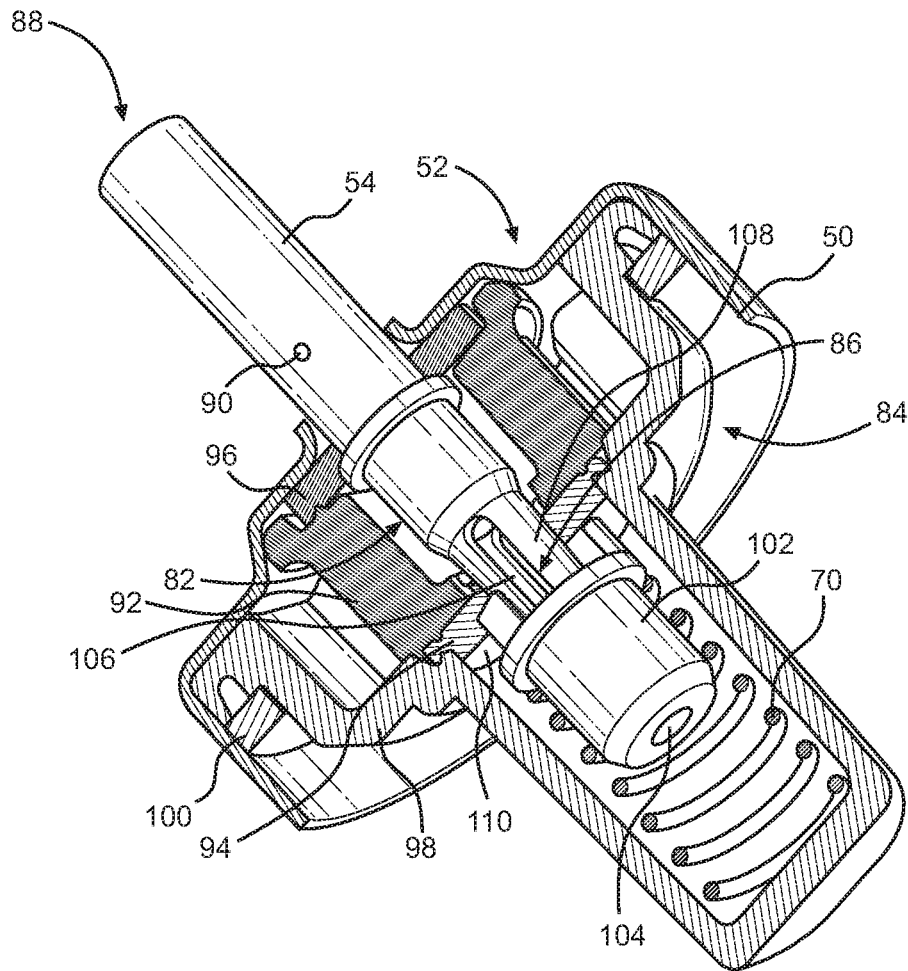


FIG. 4

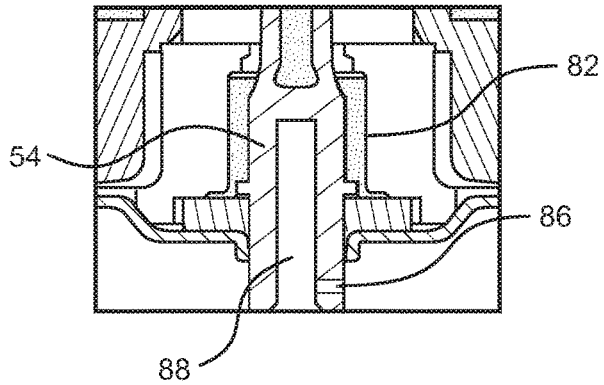


FIG. 5A

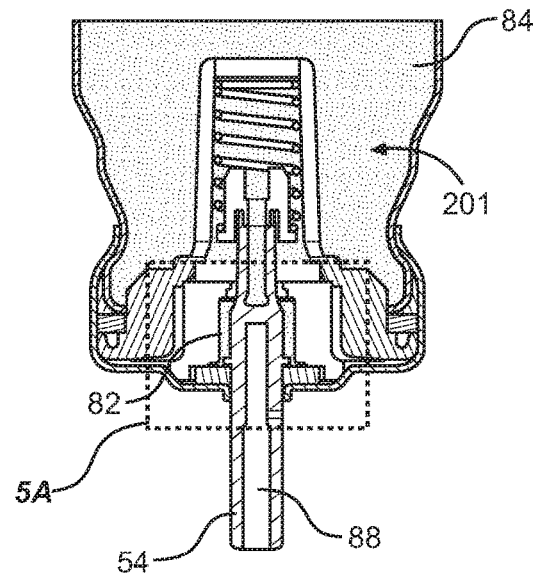


FIG. 5B

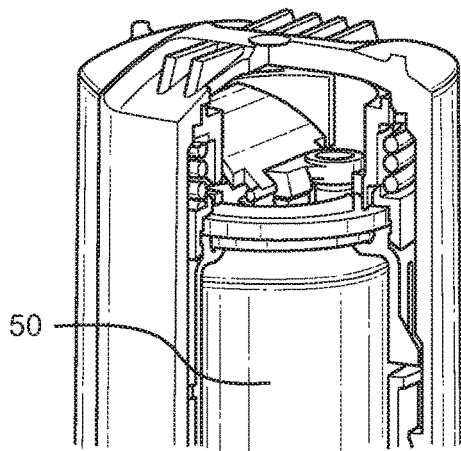


FIG. 5C

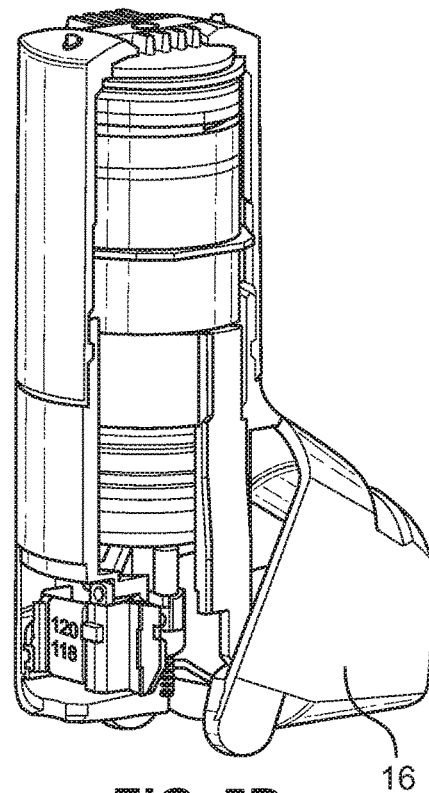


FIG. 5D

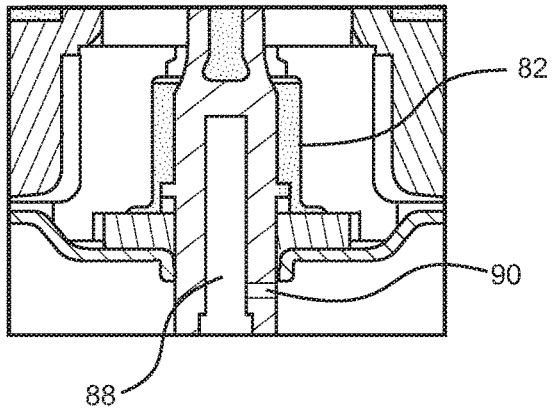


FIG. 6A

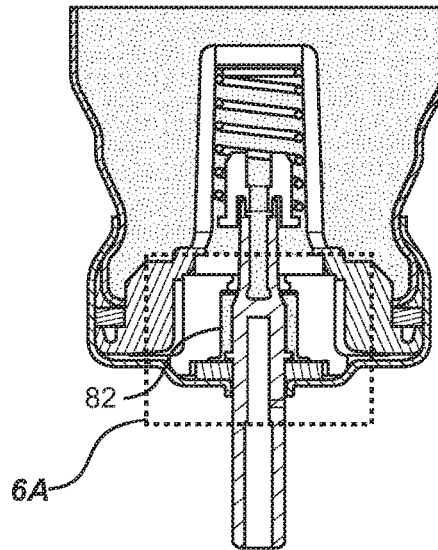


FIG. 6B

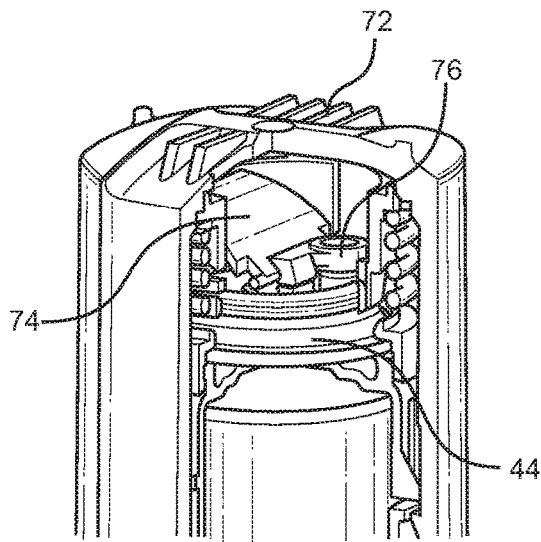


FIG. 6C

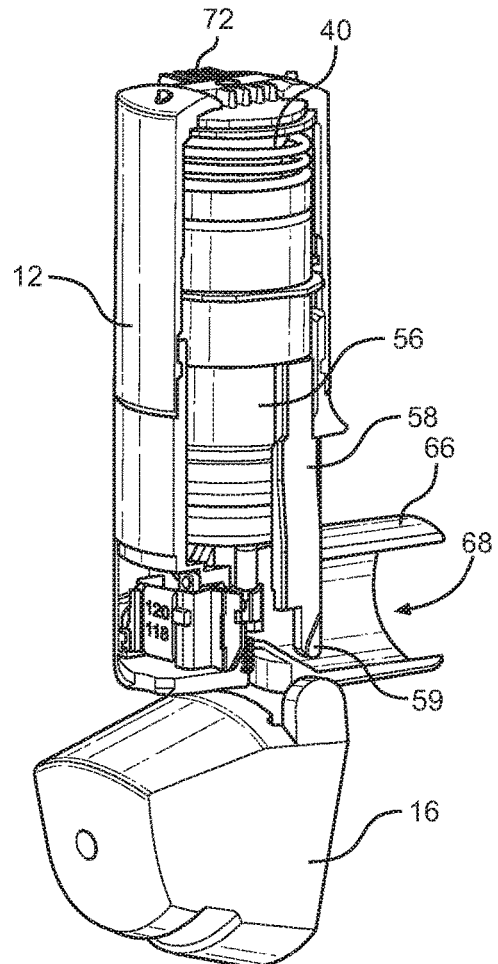


FIG. 6D

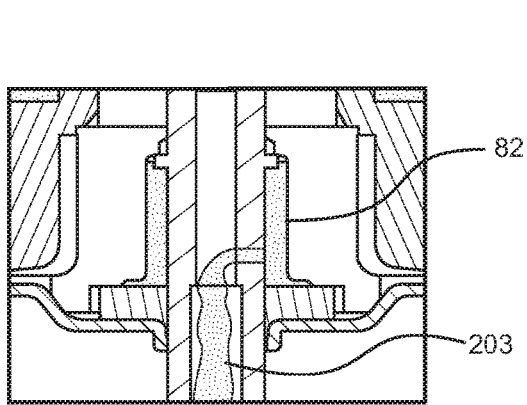


FIG. 7A

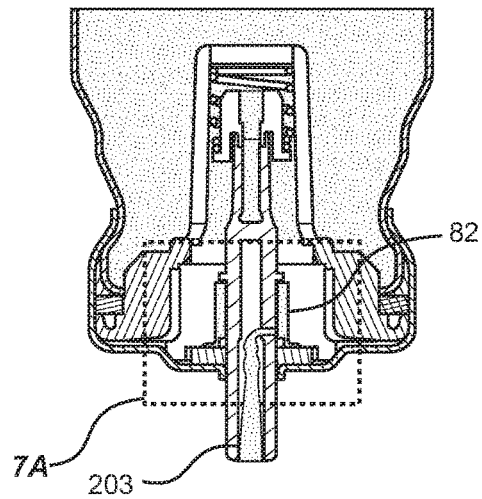


FIG. 7B

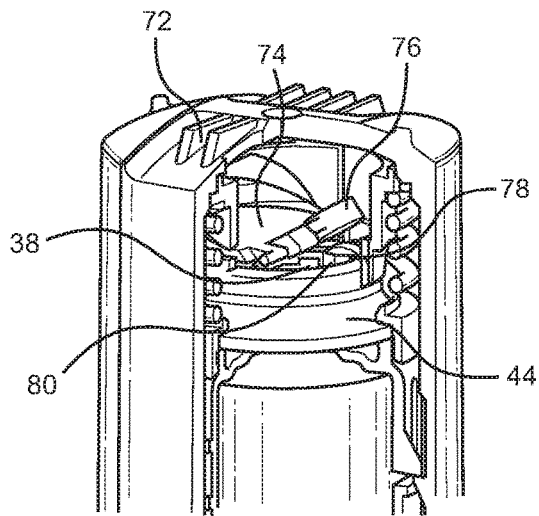


FIG. 7C

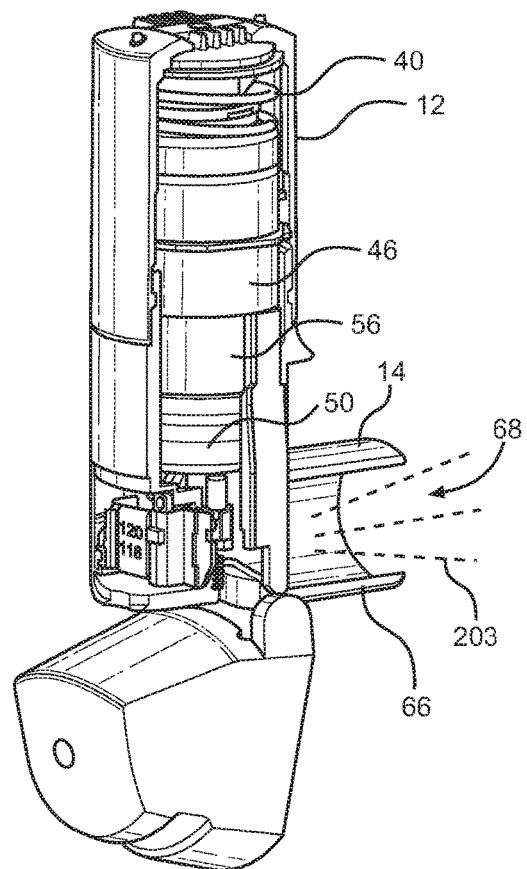


FIG. 7D

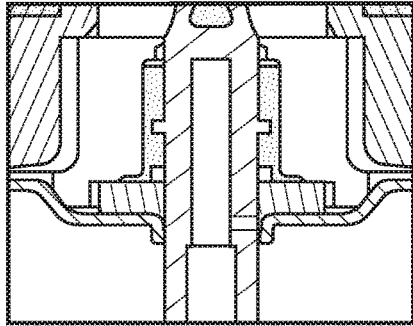


FIG. 8A

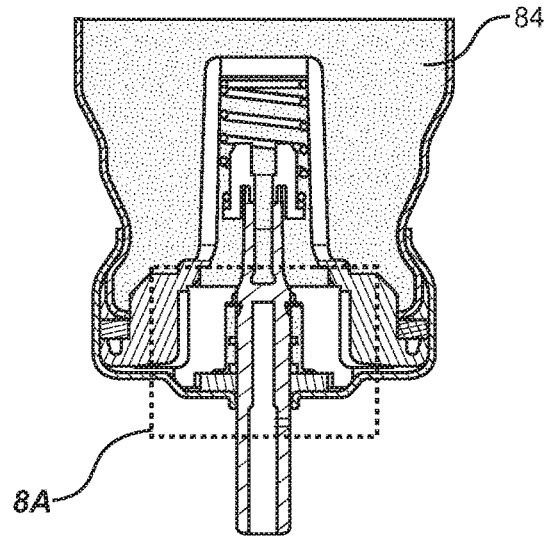


FIG. 8B

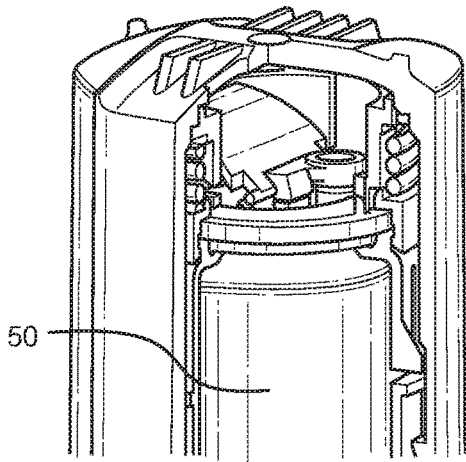


FIG. 8C

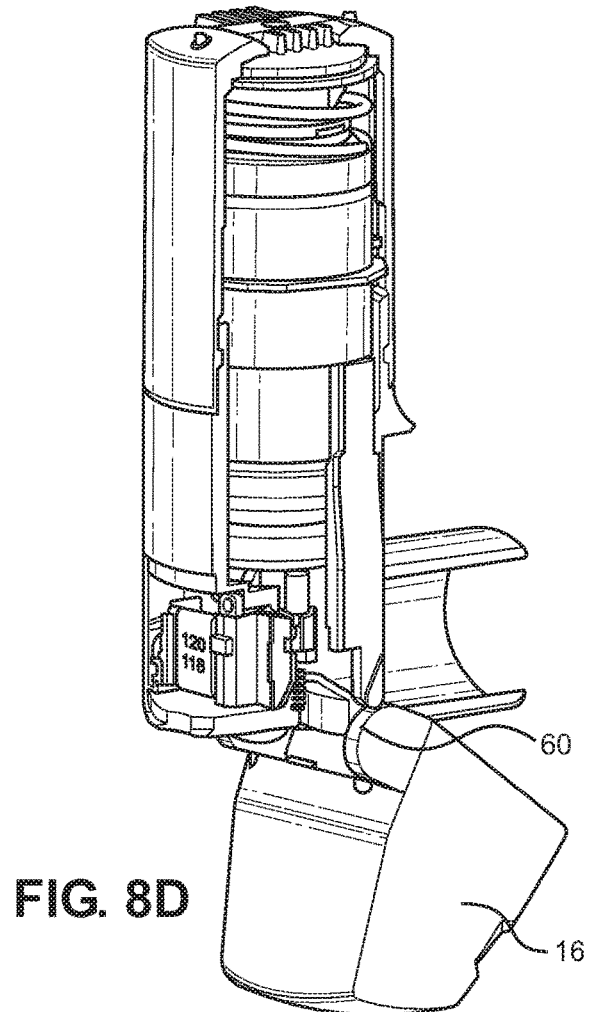


FIG. 8D

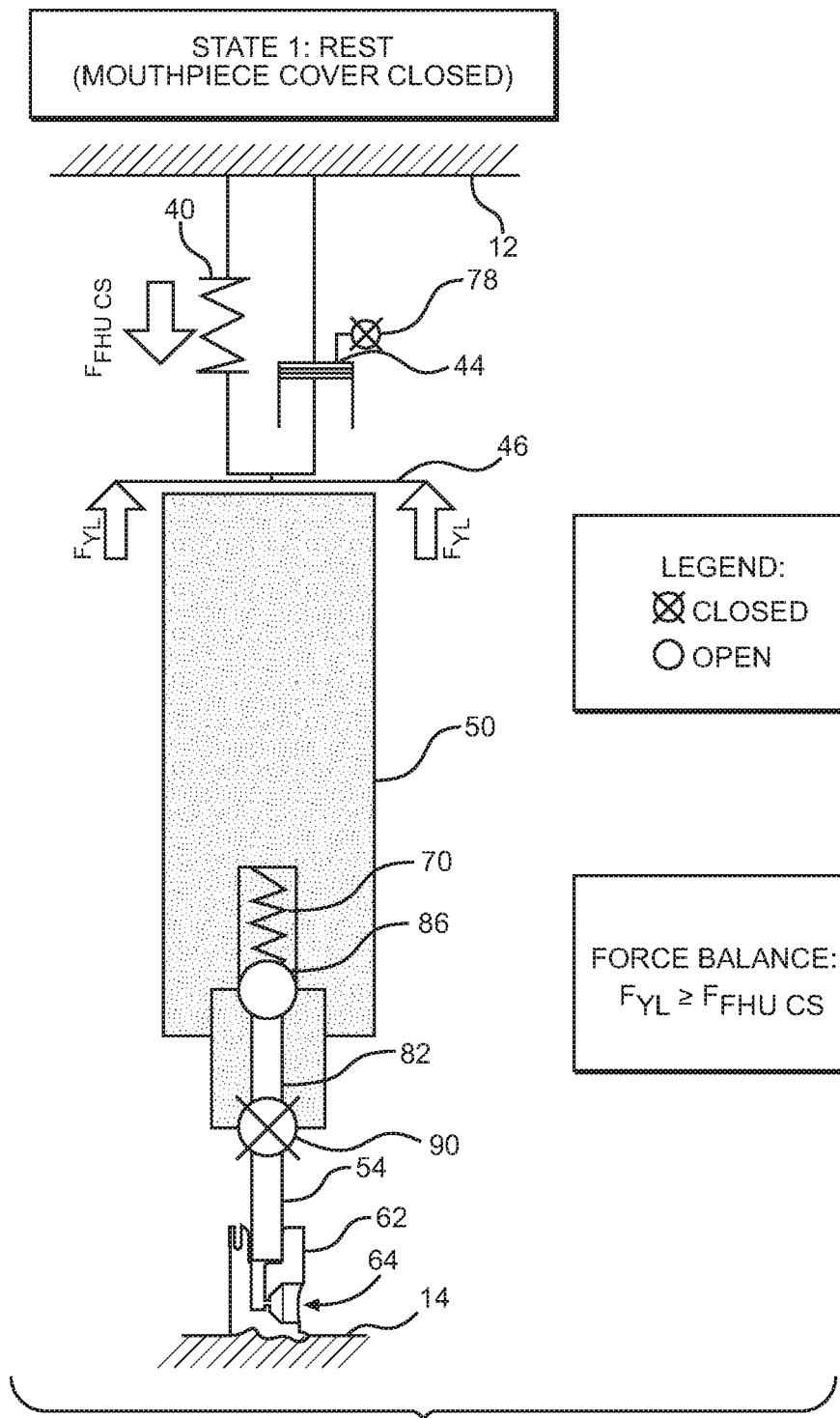


FIG. 9

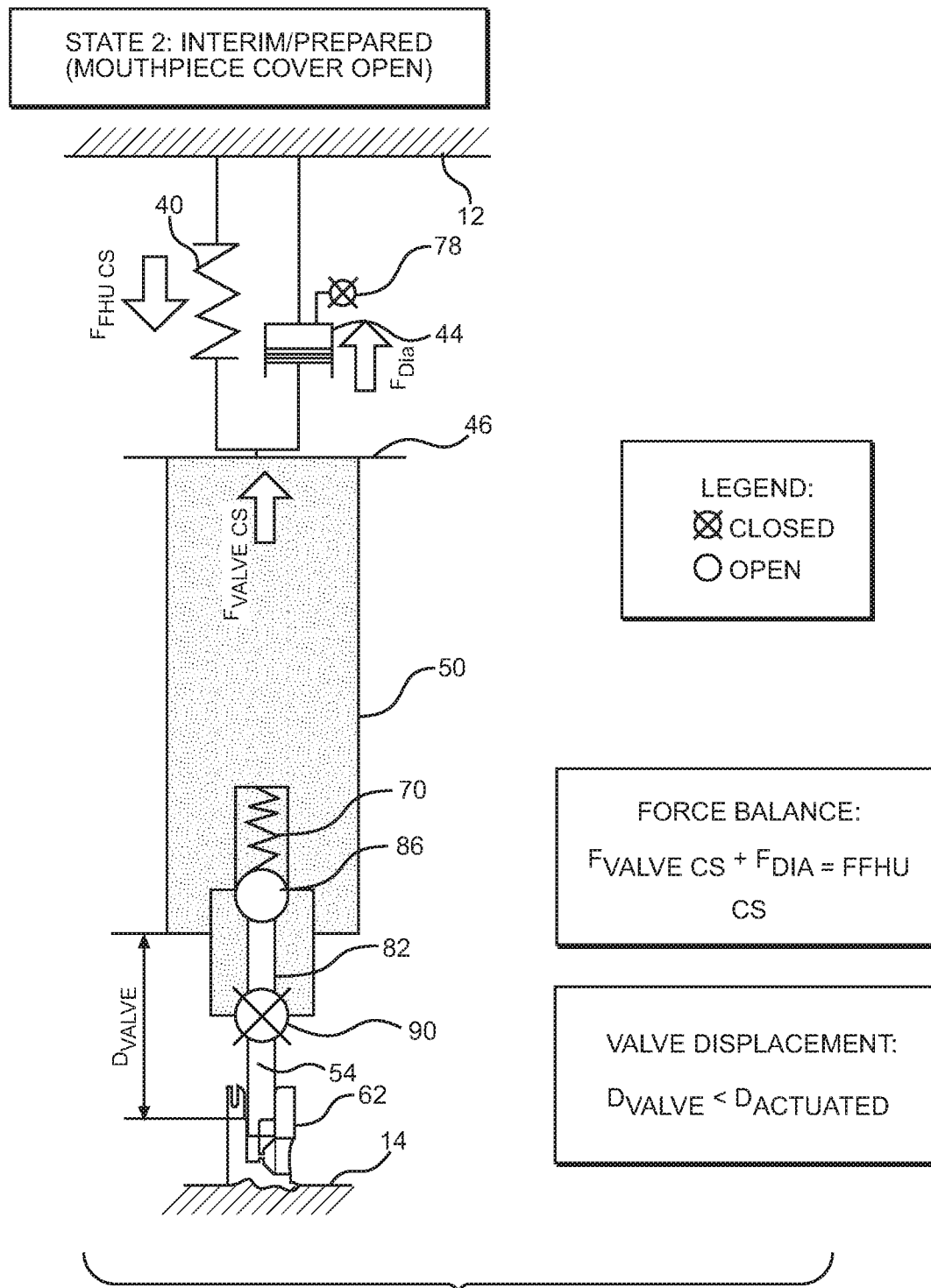


FIG. 10

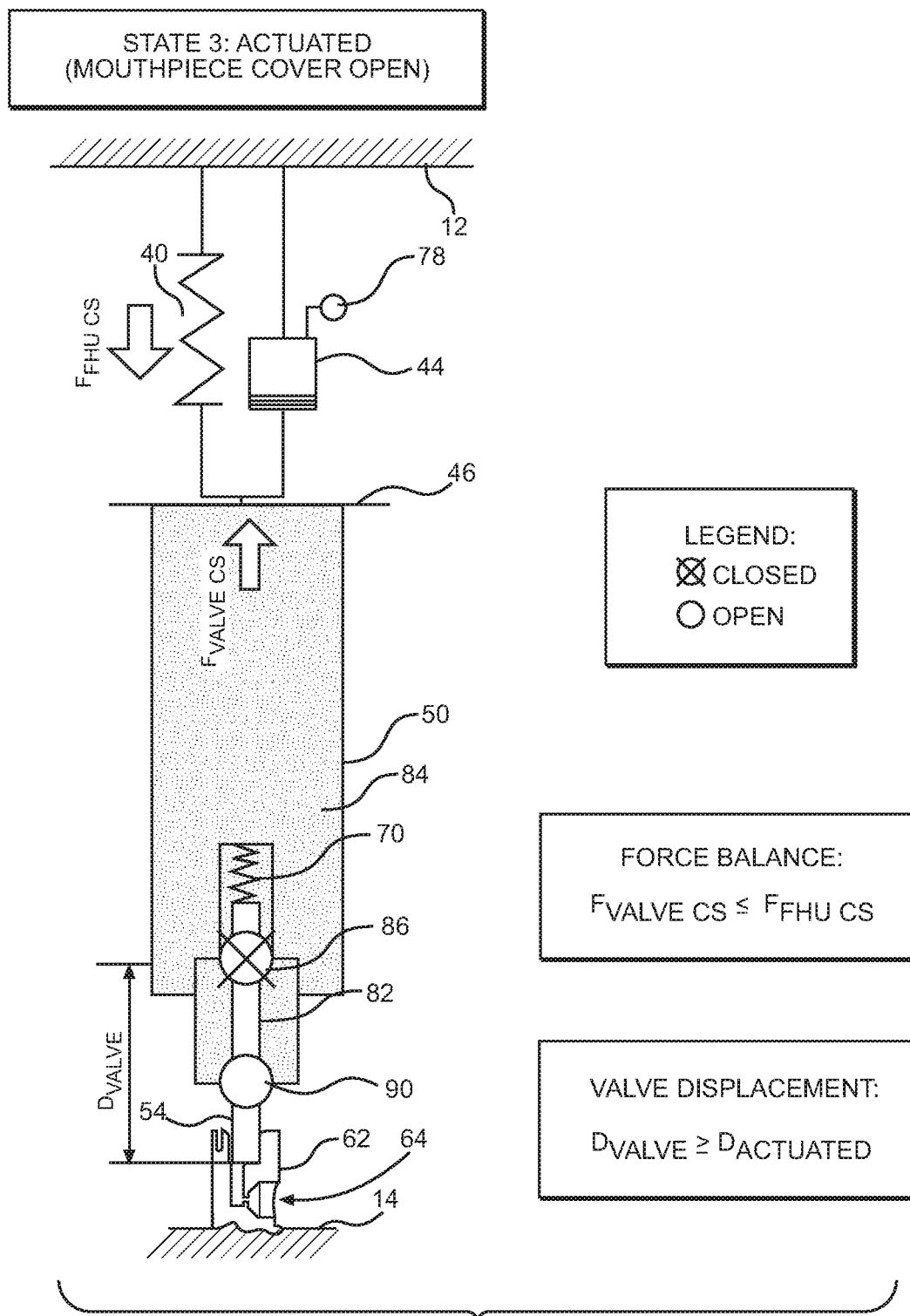
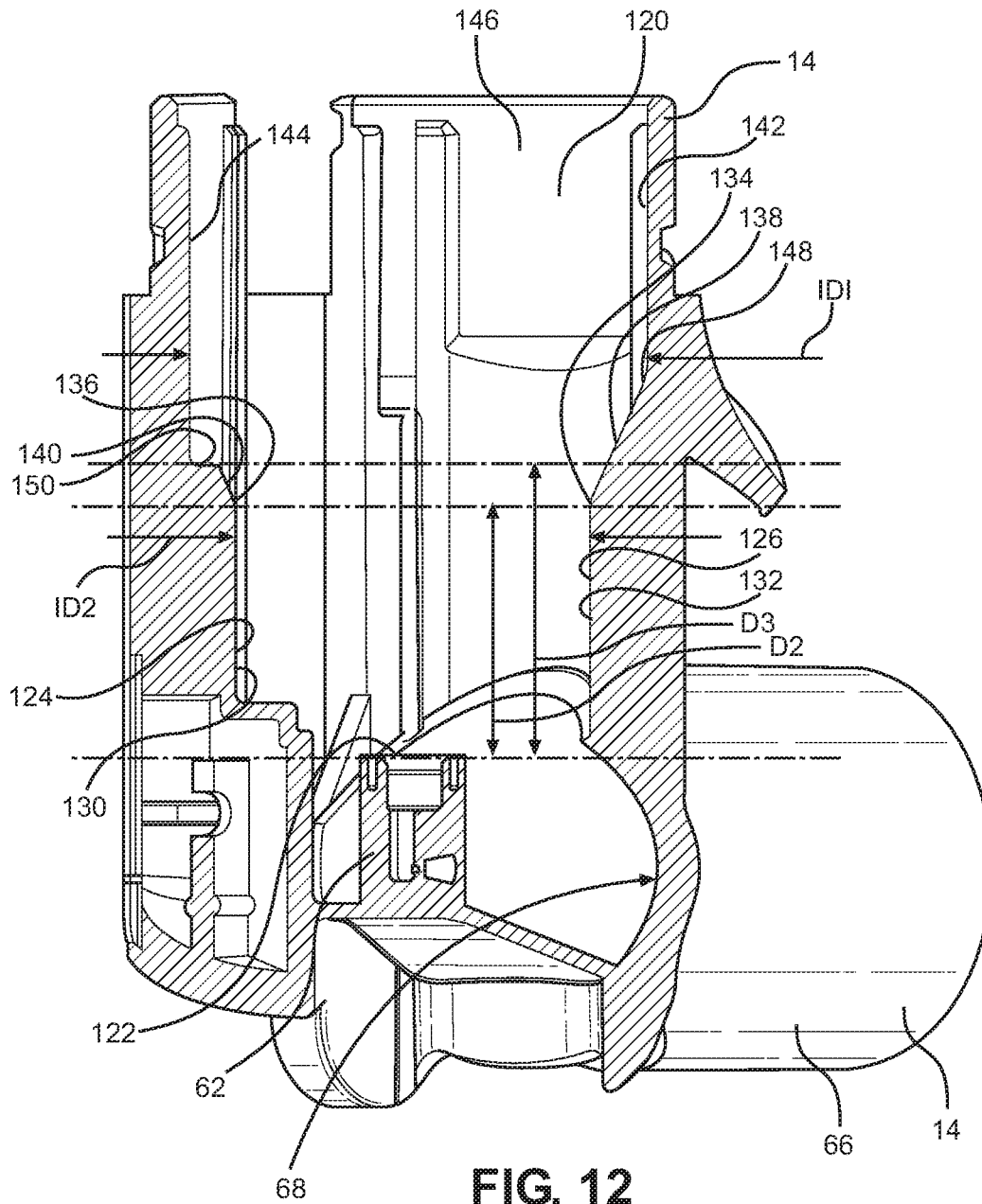


FIG. 11



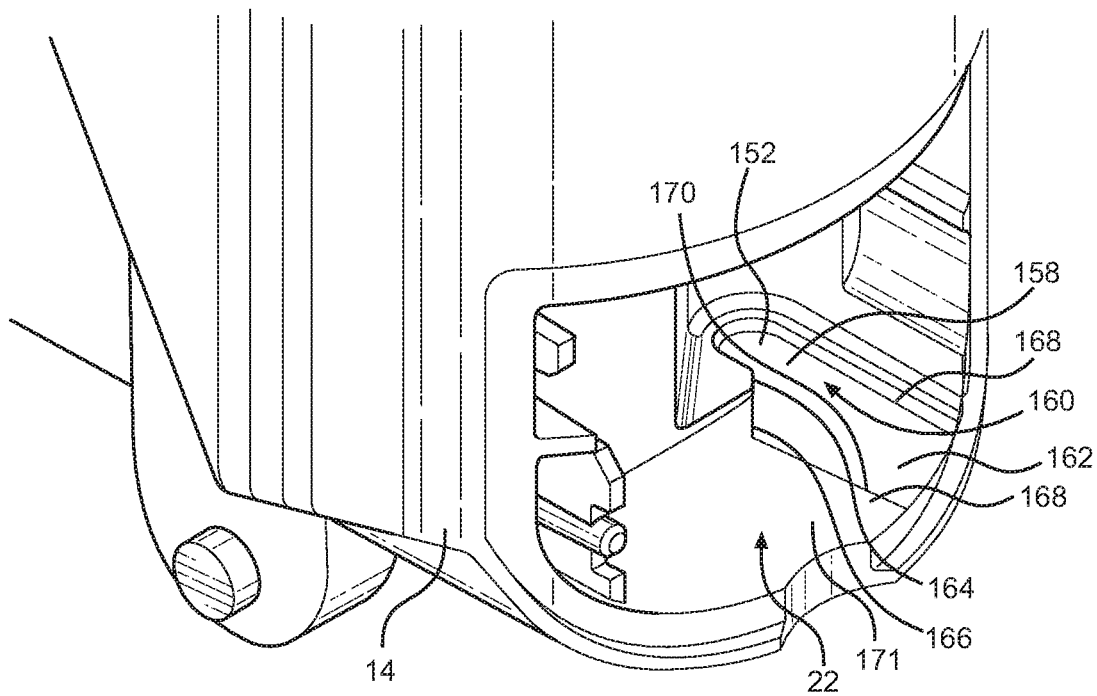
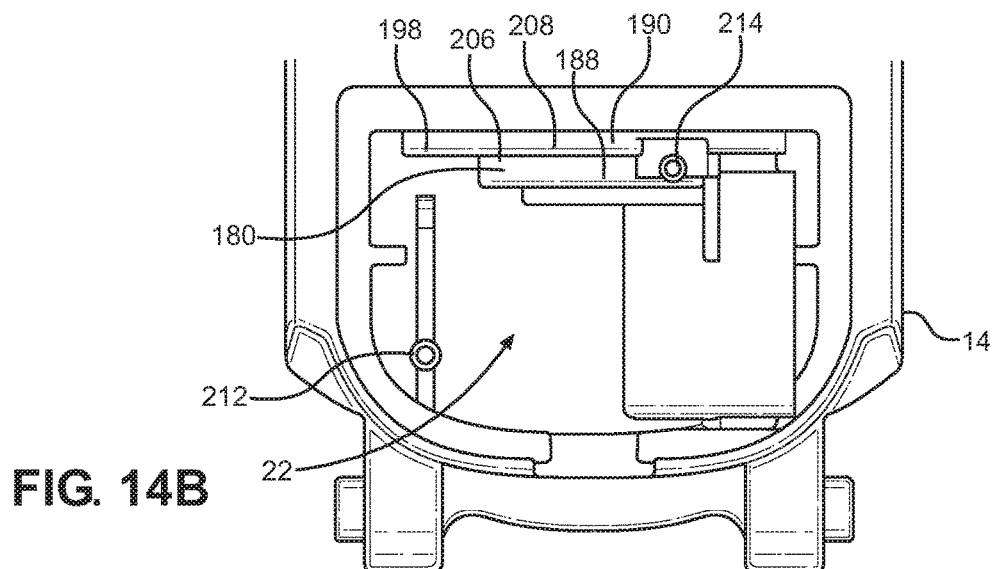
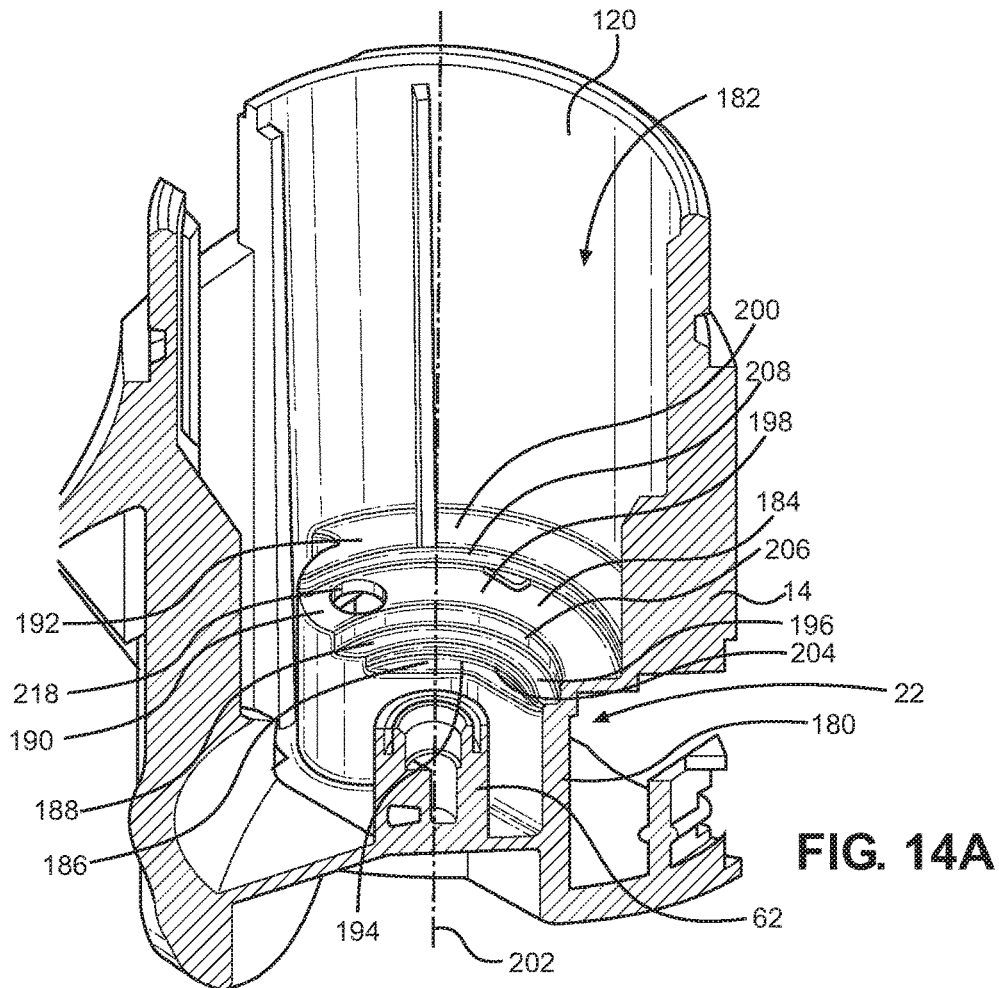


FIG. 13



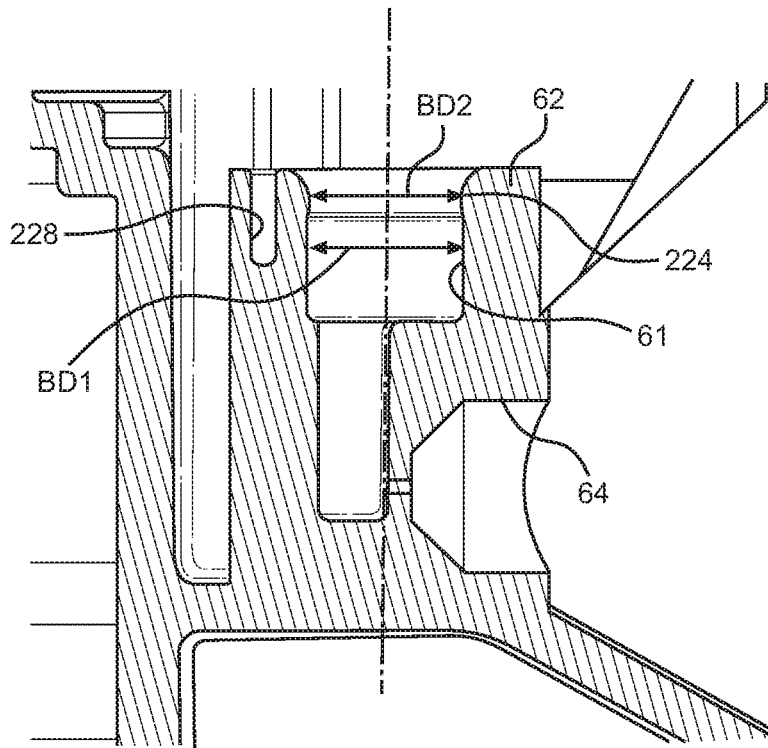


FIG. 15A

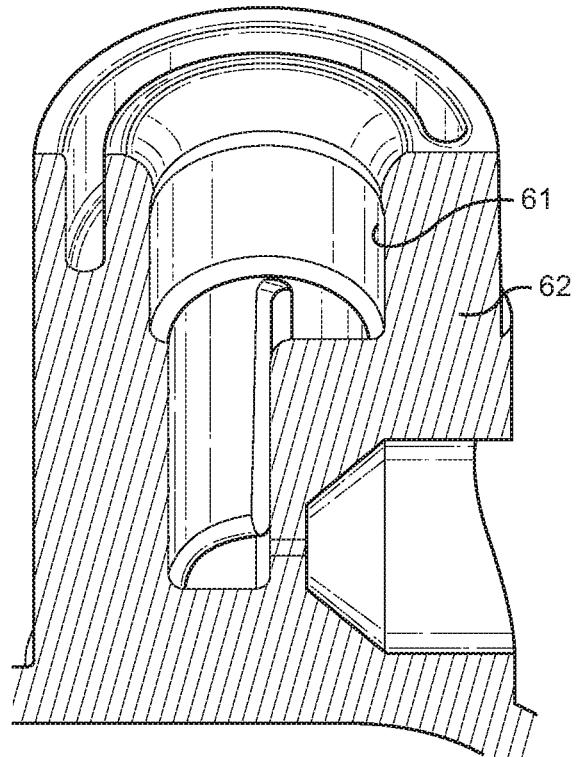


FIG. 15B

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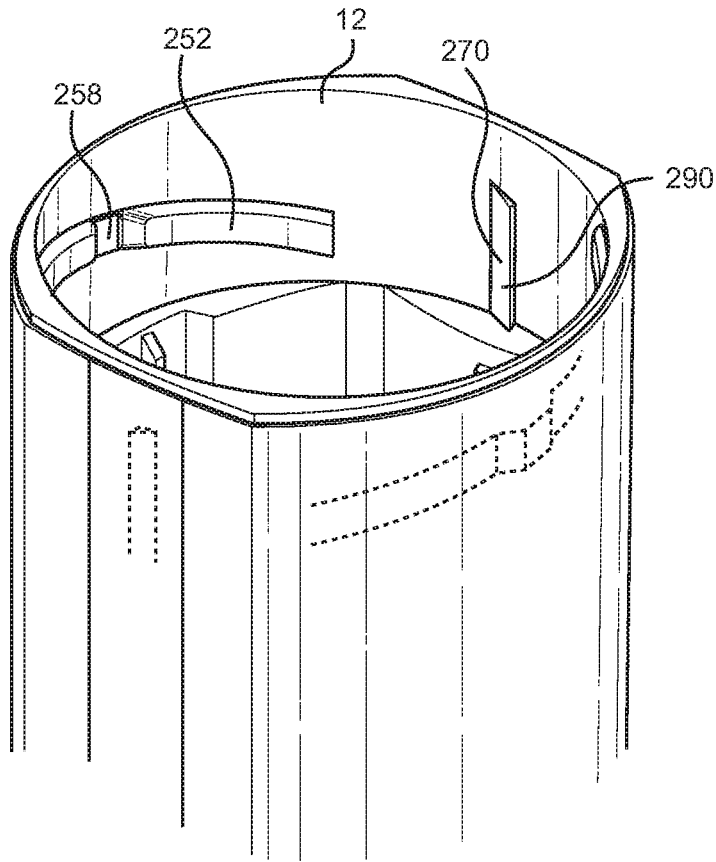


FIG. 16A

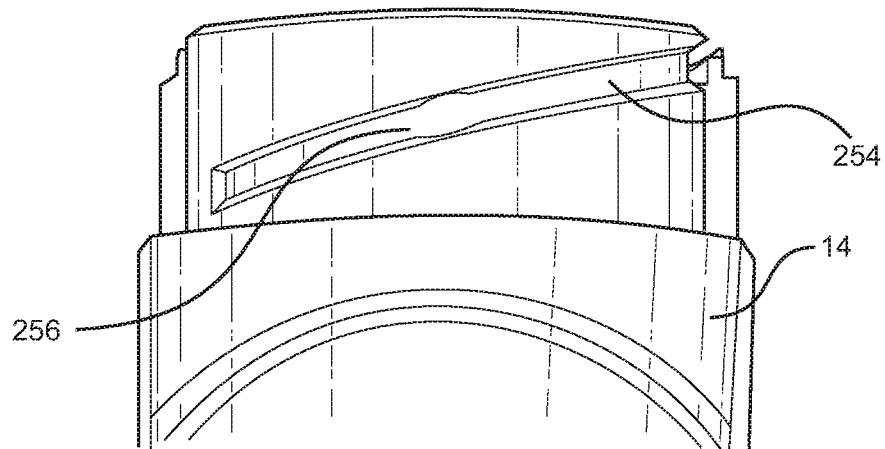


FIG. 16B

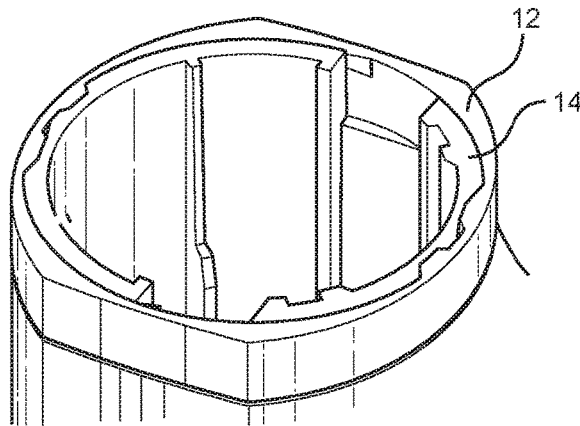


FIG. 17A

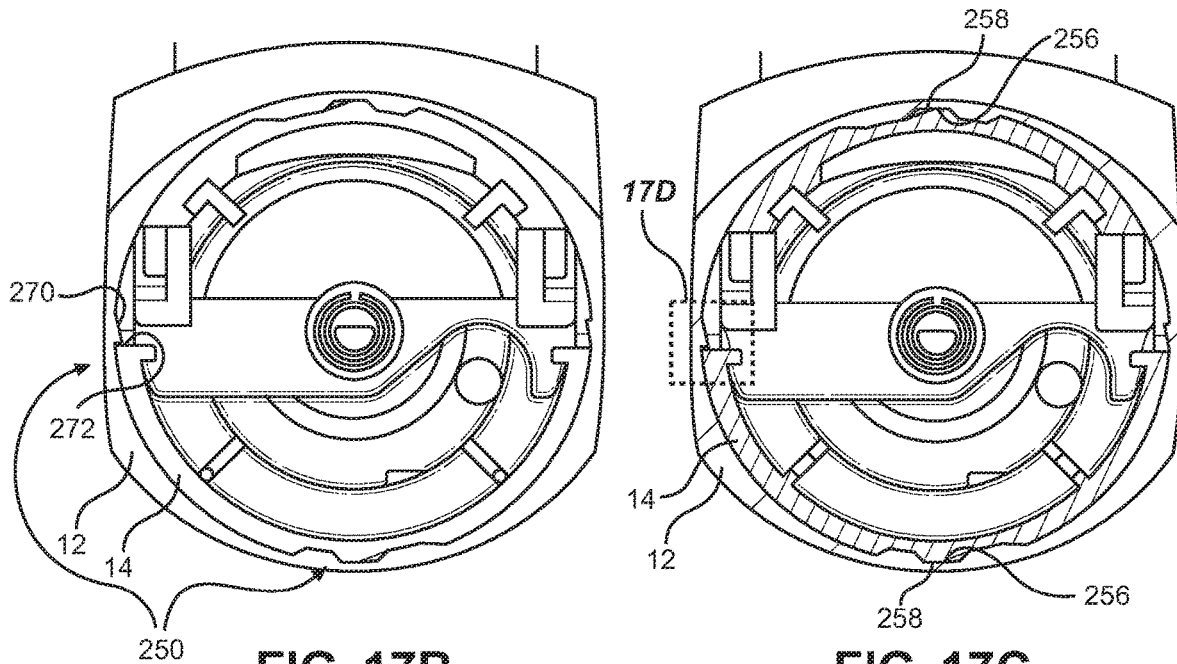


FIG. 17B

FIG. 17C

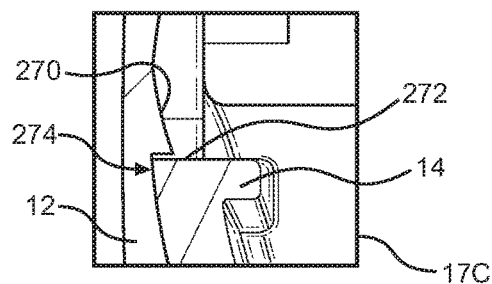
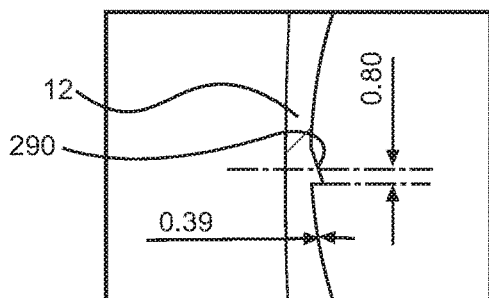
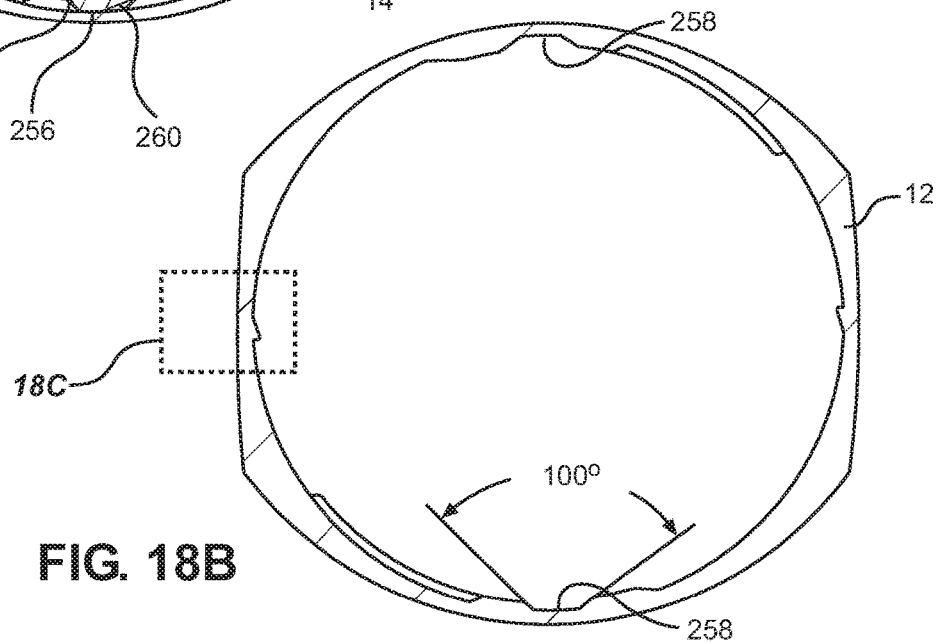
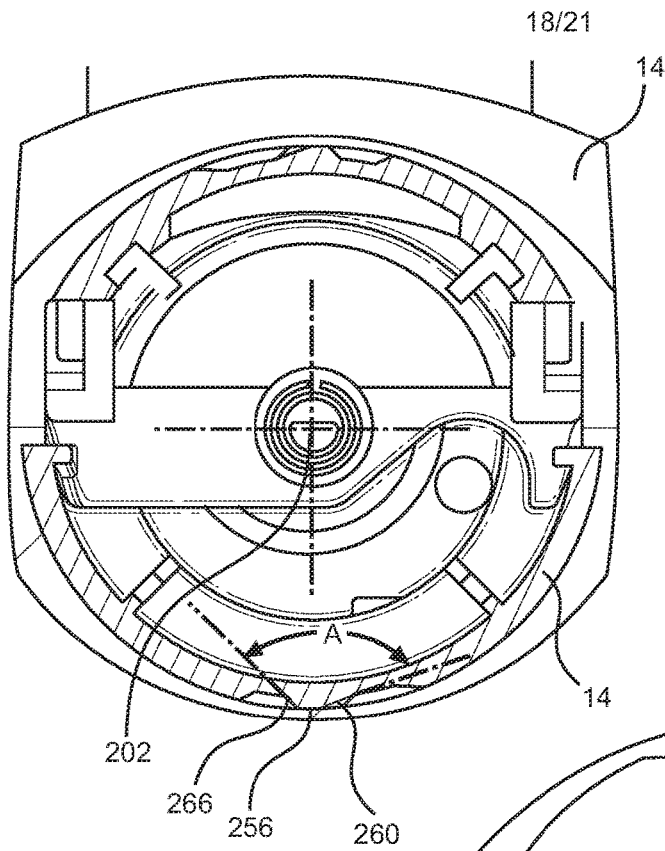


FIG. 17D



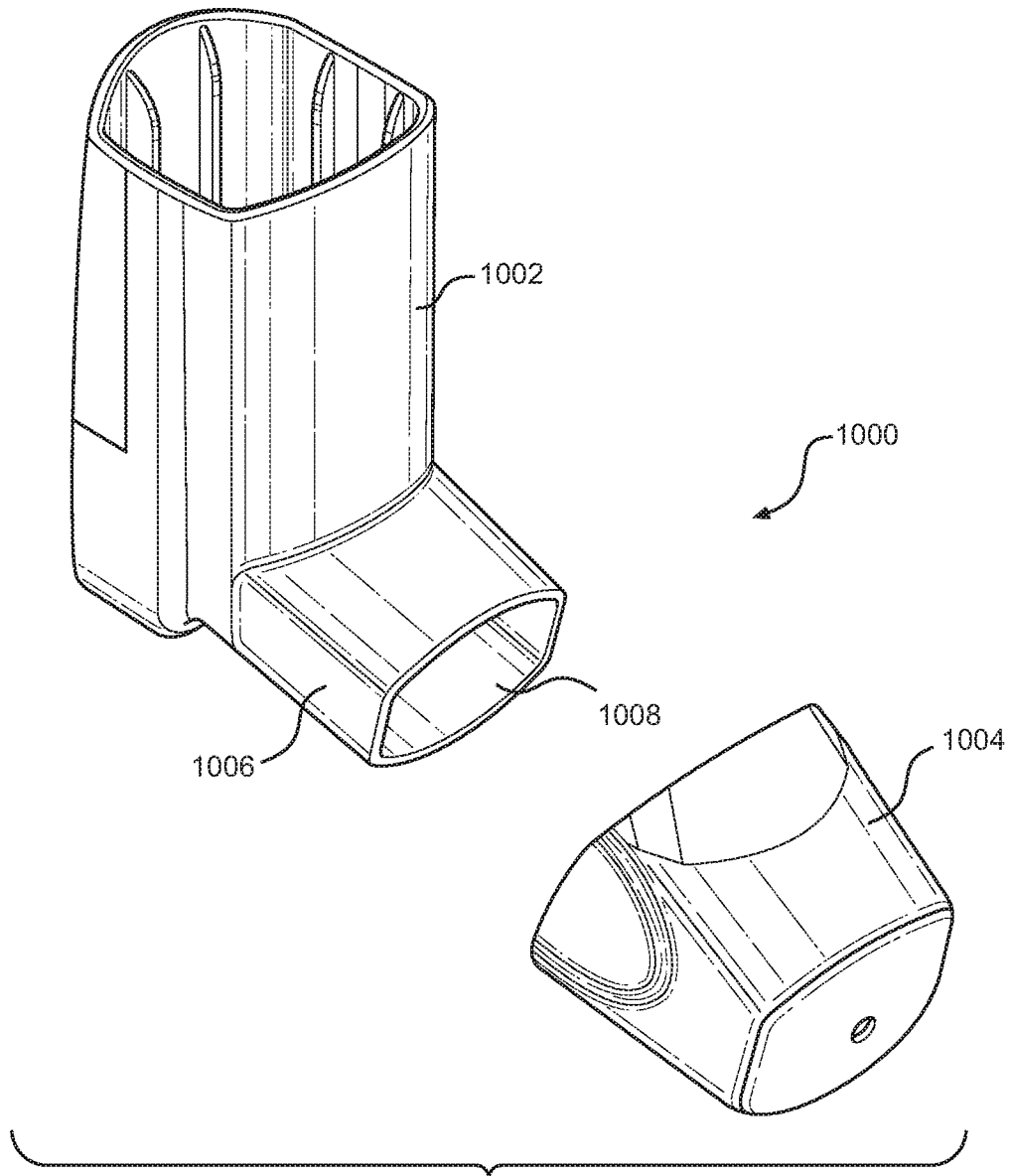


FIG. 19

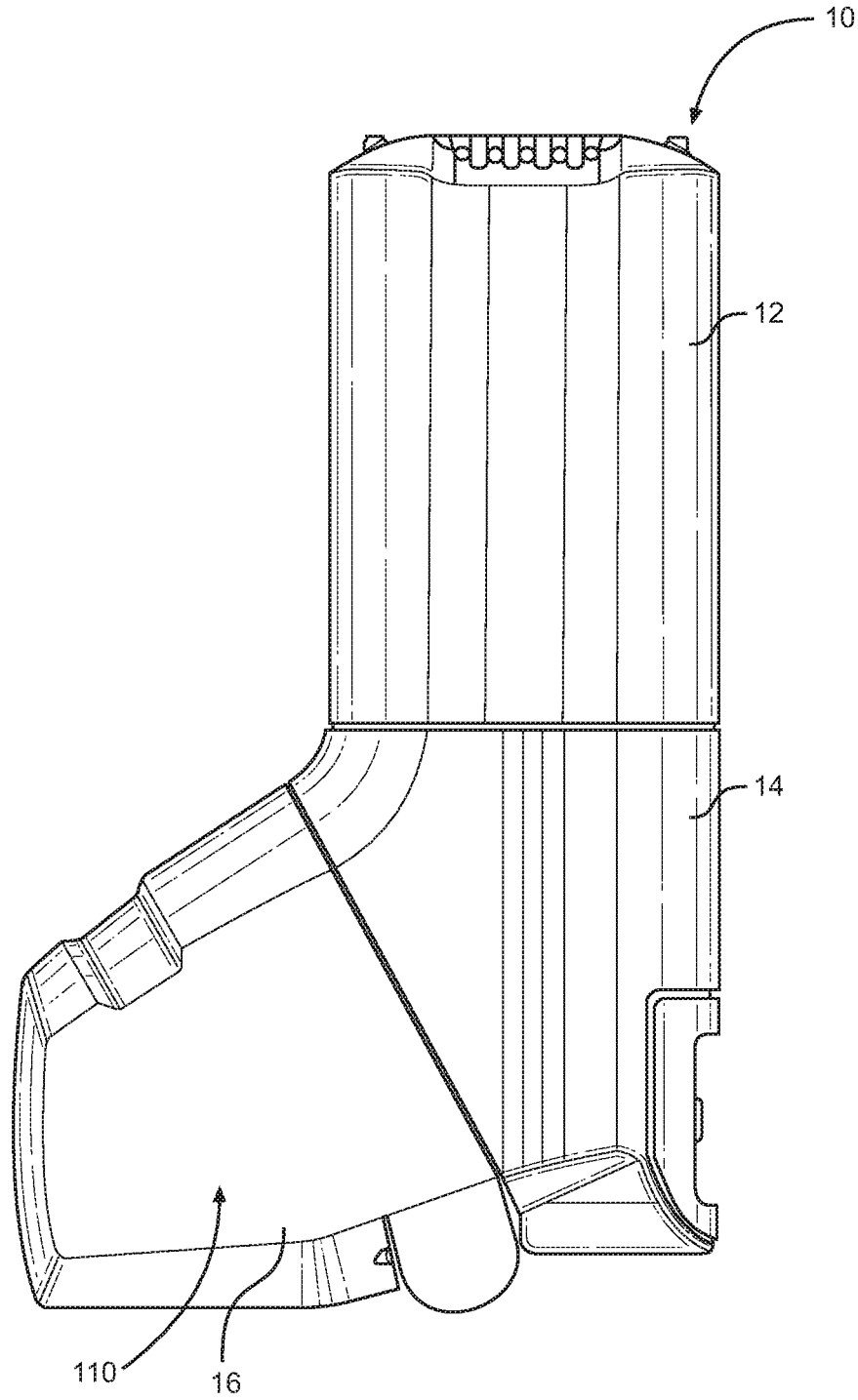


FIG. 20

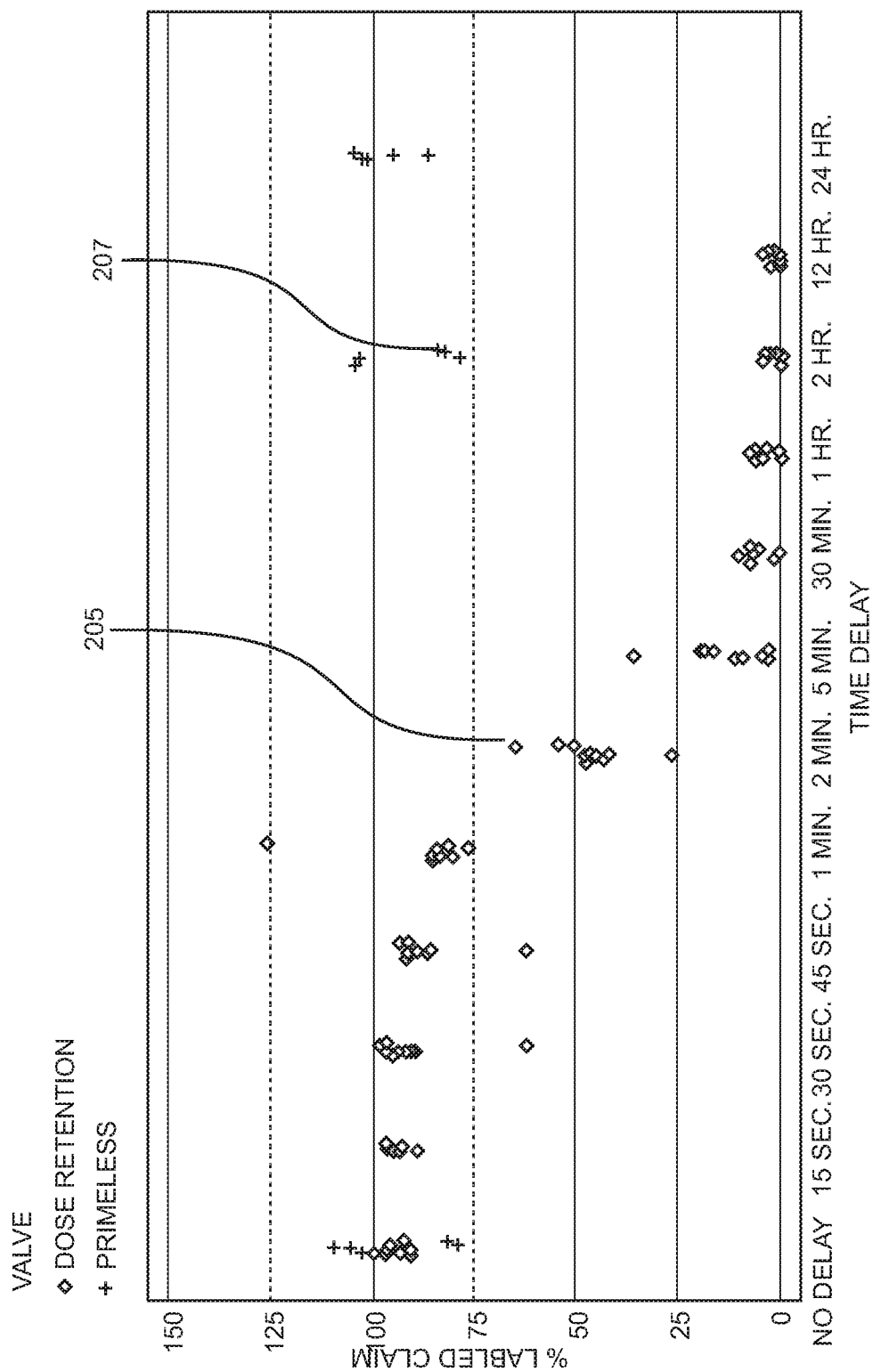


FIG. 21

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INHALERS AND RELATED METHODS

CROSS-REFERENCE TO RELATED APPLICATIONS

This application claims the benefit of priority of application No. GB1702408.4, filed Feb. 14, 2017, which application is incorporated by reference herein, in its entirety and for all purposes.

FIELD OF THE INVENTION

The present invention relates to inhalers, including breath actuated and metered dose inhalers. The invention relates to oral and nasal inhalers. The invention also relates to methods of metering inhalable substances in metering valves of canisters for medicament inhalers, inhaler housings and inhaler valve stem and valve stem block interfaces.

BACKGROUND OF THE INVENTION

A known inhaler, which is a breath actuated inhaler, has a pressurised canister and a metering valve for controlling the ejection of inhalable substances from the canister. The canister is operable by a force holding unit having a cap housing attachable to a main housing of the inhaler. The metering valve includes a valve stem for transferring substances from an interior reservoir of the canister into the metering chamber and then out of the metering chamber along the valve stem in the direction of a nozzle of the inhaler. A radially directed capillary port is provided in the valve stem for communicating substances out of the interior reservoir for communication along the valve stem to the metering chamber and a similar port is provided for communicating substances out of the metering chamber and along the valve stem towards the nozzle. In use, a mouthpiece cap is opened to ready the inhaler for inhalation and then after inhalation the mouthpiece cap is closed and resets a canister fire system. It has been found that the inhaler can be left after inhalation with the mouthpiece dust cap in the opened position with the metering chamber communicating with atmosphere via the valve stem and nozzle. This can result in the variance of active ingredients in at least one subsequent dose. This means that users will sometimes remove a force holding unit cap housing from the main body of the inhaler and try to ensure that the metering chamber is sufficiently primed by firing a number of doses and this is both wasteful and may result in damage to the inhaler.

In some inhalers, when it is necessary to make changes to internal components, it is difficult to provide space and good guidance for all the necessary interior moving parts. Also, the assembly of some inhaler dose counters can be difficult.

Furthermore, in some inhalers, despite a tight connection between the valve stem and a valve stem block within the main body, blowback can occur which is leakage of substances between the valve stem block and valve stem. It can also be difficult in some inhalers to achieve reliable dose counting to reflect the number of doses actually provided by the inhaler.

The present invention aims to alleviate at least to a certain extent at least one of the problems of the prior art.

Alternatively, the present invention aims to provide a useful inhaler, method of metering substances in a metering valve of a canister for a medicament inhaler and/or useful inhaler parts.

SUMMARY OF THE INVENTION

One aspect of the present disclosure discloses a breath actuated inhaler having a main body for accommodating a

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medicament reservoir, a canister fire system for moving the canister to release a dose in response to air flow, a cap housing for enclosing the canister fire system and canister within an interior chamber defined by the main body and the cap housing, wherein a lock system is provided for locking the cap housing on the main body.

Advantageously, a user can be prevented from tampering with and damaging the interior components of the inhaler. In the case of a breath actuated inhaler, this is particularly advantageous because prior inhalers have required the ability to remove the cap housing for manual priming of the metering chamber. But, when a metering valve is provided with an opening configured to permit flow in a direction with an axial component along the valve stem directly between the transfer space inside the valve stem and the interior reservoir, and when the interior reservoir is arranged for orientation above the metering chamber whereby gas such as air located within the metering chamber is replaced with liquid from the interior reservoir, it is no longer necessary to be able to open the inhaler for manual priming of the metering chamber by manually pushing and firing the canister.

Helical threads may be provided for rotational attachment of the cap housing on the main body and for resisting relative longitudinal movement therebetween without rotation.

The lock system may include a protrusion in the region of a helical thread on one of the main body and the cap housing which is lockable in a recess in the region of a helical thread on the other of the main body and the cap housing.

Two said protrusions may be engageable in two said recesses formed at opposing locations on the inhaler.

Each protrusion may have a leading ramp surface and a trailing ramp surface, the included angle between the ramp and trailing surfaces being about 95° to 120°; the included angle of the protrusion preferably being larger than that of the recess.

The main body may have a central axis and the ramp surfaces are inclined at an angle of about 45° plus or minus 15° (or plus or minus 10°) to tangential.

The lock system may include a first lock member on one of the main body and the cap housing which is adapted to engage a second lock member at a lock interface formed by respective engagement faces thereof, the lock interface being oriented substantially perpendicular to tangential.

The main body may have a central axis and the first lock member has a radial extent of 0.25 to 0.75 mm, preferably about 0.35 to 0.45 mm; the first lock member preferably having a longitudinal extent of about 10 mm.

The main body and the cap housing may be formed of plastics material and the lock system may be configured so that a release torque required to overcome the locking provided by the plastics main body and cap housing is more than 1 Nm.

The lock system may be configured such that the release torque is between 2 and 5 Nm, preferably between 2.5 and 3 Nm, about 2.7 Nm being one example.

According to another, the present disclosure discloses a method of metering inhalable substances in a metering valve of a canister for a medicament inhaler, the method comprising: providing the metering valve with a metering chamber and valve stem extending from a metering chamber to an interior reservoir of the canister, with the valve stem defining a communication path between the metering chamber and the interior reservoir, the communication path including an opening configured to permit flow between a transfer space inside the valve stem and the interior reservoir; and orienting

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the interior reservoir above the metering chamber and replacing gas such as air located within the metering chamber with liquid from the interior reservoir.

The present inventors have worked out that the reasons why inaccurate dosing can occur include that when the metering chamber is left vented to atmosphere in some prior inhalers for as little as 2 minutes, a gas or air lock can form in the metering chamber and when the metering chamber is next connected for communication with the interior reservoir, due to the radial capillary port, the gas or air is trapped within the metering chamber and liquid does not enter the metering chamber reliably as the next dose. The air may enter the metering chamber from the atmosphere in the prior art. This may happen as propellant in the metering chamber evaporates and diffuses into the atmosphere. Using the presently disclosed method which involves the use of the opening configured to permit flow in a direction with an axial component along the valve stem directly between a transfer space inside the valve stem and the interior reservoir, when the interior reservoir is oriented above the metering chamber, this enables liquid from the interior reservoir to replace gas such as air located within the metering chamber and an accurate dose can be administered at the next dose.

The opening may be configured to permit flow in a direction with an axial component along the valve stem directly between the transfer space inside the valve stem and the interior reservoir.

The replacing gas located in the metering chamber with liquid from the interior reservoir may include flowing liquid under pressure through the opening, along the valve stem to a portion of the communication path communicating with the metering chamber.

The method may include flowing gas from the metering chamber, in a direction counter to a direction of liquid flow from the interior reservoir, along the communication path into the interior chamber.

The method may include providing the opening as an elongated opening.

The method may include providing a second opening to the communication path diametrically opposed to the first said opening.

The method may include providing the valve stem with at least one said opening into the interior reservoir as having an axially oriented opening portion which is oriented facing directly axially along a longitudinal axis of the valve stem into the interior reservoir, and which includes flowing liquid into the metering chamber via said axially oriented opening portion.

The method may include venting the metering chamber to atmosphere via a valve stem block and/or nozzle.

The method may include operating the metering valve and canister within a medicament inhaler and holding the valve stem depressed relative to the canister with the metering chamber vented to atmosphere so as at least partially to permit substances within the metering chamber to vaporise and to permit atmospheric air to enter the metering chamber.

Advantageously, the inhaler can be left for a long period such as 24 hours with the metering chamber communicating with atmosphere and then when the metering chamber is reconnected to the interior reservoir and the interior reservoir is oriented above the metering chamber the metering chamber can fully fill with liquid for the next dose. Advantageously, in a breath actuated inhaler, the features of the method mean therefore that any force holding unit and/or cap housing for the inhaler can be permanently secured or locked on to the inhaler so that users cannot tamper with the

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interior and there is no need to perform manual priming of the metering valve, which is a necessity in prior art inhalers, before the next dose is taken.

The method may include providing the medicament inhaler as a breath actuated inhaler, and may include, in response to air flow, firing the canister by closing communication between the metering chamber and interior reservoir and opening communication between the metering chamber and atmosphere, the valve stem being held depressed after firing.

The method may include resetting the inhaler to a reset configuration with a reset actuator so as to close communication between the metering chamber and atmosphere and open communication between the metering chamber and the interior reservoir, and carrying out the orienting of the interior reservoir above the metering chamber while the inhaler is in the reset configuration.

The method may include providing the reset actuator as a lever, press button, hinged or rotatable piece, dust cap, nasal outlet cap or mouthpiece cap for the inhaler. Closing the actuator may reset the inhaler. In the case of an oral inhaler the reset actuator may be a dust cap mouthpiece cap. In the case of a nasal inhaler, the reset actuator may take a variety of forms, including but not limited to a dust cap or a movable lever, cap or button. In this case, the carrying out of the orienting of the interior reservoir above the metering chamber being carried out once the reset actuator has been opened to a configuration suitable for inhalation or otherwise operated. Therefore, it can be ensured that right before inhalation, the metering chamber is full of liquid and any gas which may have been in the metering chamber has been drawn into the interior reservoir due to the free flowing communication pathway between metering chamber and interior reservoir.

In an alternative embodiment, the inhaler may include a dust cap or mouthpiece cap which closes communication between the metering chamber and atmosphere but does not reset the inhaler. In these cases, optionally, a separate reset actuator may be provided.

The method may include providing the medicament inhaler as a metered dose inhaler and may include applying a force to the canister to hold the valve stem depressed; and may include subsequently releasing the canister to extend the valve stem and carrying out the orienting of the interior reservoir above the metering chamber.

The method may include providing the inhalable substances as including at least one propellant.

The method may include providing at least one said propellant as a hydrofluoroalkane, such as 1,1,1,2-tetrafluoroethane.

The method may include providing at least one said propellant with a surface tension at 25° C. of about 6 to 10 mN/m, typically about 7 to 9 mN/m, about 8 mN/m being one example.

Advantageously, it has been found that fluid with this surface tension is capable of avoiding gas or air lock in the metering chamber by flowing into the metering chamber when the features of the presently disclosed method are used.

The method may include providing the inhalable substances as including an active ingredient in suspension or in solution, such as beclomethasone dipropionate or tiotropium bromide.

According to a further aspect, the present disclosure discloses a breath actuated inhaler for the inhalation of inhalable substances, the inhaler comprising: a canister having an interior reservoir containing pressurised inhalable

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substances including fluid; a metering valve including a metering chamber and a valve stem defining a communication path between the metering chamber and the interior reservoir, the communication path including an opening configured to permit flow between a transfer space inside the valve stem and the interior reservoir, the interior reservoir being arranged for orientation above the metering chamber whereby gas such as air located within the metering chamber is replaced with liquid from the interior reservoir.

Advantageously, with this configuration of metering valve there is no need to manually prime the metering chamber by repeatedly firing the canister manually and an accurate next dose can be provided to the metering chamber since a gas or air lock can be avoided. This also means, advantageously, that in a breath actuated inhaler having a force holding unit or cap housing secured to a main body of the inhaler, these components may be locked together so that it is relatively difficult for a user to remove the force holding unit or cap housing and tamper with the interior components. Instead, there is no need to perform manual priming and the inhaler main housing and the cap housing can be permanently locked together enclosing the internal moving parts of the inhaler where they cannot easily be damaged.

The opening may be configured to permit flow in a direction with an axial component along the valve stem directly between a transfer space inside the valve stem and the interior reservoir.

The communication path may be configured to permit liquid to flow under pressure along the communication path to the metering chamber and gas to flow in a reverse direction therealong from the metering chamber into the interior reservoir.

The opening may comprise an elongated opening.

The inhaler may include a second opening or further openings into the communication path.

The second opening may be diametrically opposed to the first said opening.

The valve stem may have at least one opening into the interior reservoir with an axially oriented portion facing directly axially along a longitudinal axis of the valve stem into the interior reservoir for the flow of fluid directly into the communication path in an axial direction along the valve stem.

The inhaler may include a metering chamber exit port for venting the metering chamber to atmosphere via a stem block and/or nozzle.

The inhaler may include a canister fire system for ejecting inhalable substances from the inhaler in response to air flow by closing communication between the metering chamber and the interior reservoir and opening communication between the metering chamber and atmosphere. The canister fire system preferably includes a drive such as a spring for driving the canister relative to the valve stem. The inhaler may have an actuator system for operating the drive, the actuator system optionally including a vacuum chamber having a vacuum release system operable to permit the drive to drive movement of the canister relative to the valve stem. The vacuum release system may be air flow actuatable.

The actuator and/or drive may include or operate as a latch, trigger or switch and may take other forms in other embodiments such as being electromechanical.

The canister fire system may be adapted to depress the valve stem into the canister to cause inhalable substances to be ejected from the inhaler and to hold the valve stem depressed with the metering chamber communicating with atmosphere.

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The canister fire system may include a reset actuator which is operable so as to extend the valve stem relative to the canister in order to close communication between atmosphere and the metering chamber and to open communication between the metering chamber and the interior reservoir.

In the case of a nasal inhaler, the reset actuator may, for example, comprise a dust cap or a lever, cap or button. In the case of an oral inhaler, the reset actuator may comprise a dust cap or mouthpiece cap for a mouthpiece of the inhaler. The mouthpiece cap may be closable to permit extension of the valve stem relative to the canister, the mouthpiece cap optionally being hingedly connected to a main housing of the inhaler for camming engagement with at least one drive rod. The drive rod may be associated with a yoke for pushing on a drive element to compress a spring of the drive.

In an alternative embodiment, the inhaler may include a dust cap or mouthpiece cap which closes communication between the metering chamber and atmosphere but does not reset the inhaler. In these cases, optionally, a separate reset actuator may be provided.

The inhaler may include a preventer adapted, after an inhalation has taken place, to prevent a further inhalation until the reset actuator has been operated to extend the valve stem. In the case of a mouthpiece or other cap, this may comprise closing the cap.

Advantageously, the preventer may therefore ensure that the user closes the cap at some time before each inhalation and this in turn means that reliable dosing can be achieved.

The preventer may comprise a warning signaler, such as an audible or visual alarm, dose counter or warning notice, quick reference guide or instructions.

The inhaler may include inhalable substances in the interior reservoir which include at least one propellant.

At least one said propellant may comprise a hydrofluoroalkane, such as 1,1,1,2-tetrafluoroethane.

At least one said propellant may have a surface tension at 25° C. of about 6 to 10 mN/m, typically about 7 to 9 mN/m, about 8 mN/m being one example.

The inhaler may include at least one inhalable substance in the interior reservoir as an active ingredient, for example in suspension or in solution, such as beclomethasone dipropionate or tiotropium bromide.

The inhaler may include a dose counter for counting doses, preferably for making one count with each inhalation of a dose.

The dose counter may include: (a) a tape bearing dose indicia for displaying counts and/or (b) an actuator pin for contact with the canister, or a body movable therewith, for counting doses, and preferably a dose counter chamber separated by a barrier from an inner space of the inhaler for containing the canister, the actuator pin optionally extending out of the dose counter chamber through an aperture in the wall for contact during counting with the canister (or the body movable therewith).

The inhaler may be a breath actuated inhaler.

The inhaler may be a metered dose inhaler.

The inhaler may be an oral inhaler.

The inhaler may be a nasal inhaler.

The inhaler may include a reset actuator which when actuated prevents exposure of the metering chamber to atmosphere, wherein the inhaler provides 75 to 125% of labelled claim for a dose following exposure of the metering chamber to atmosphere for a time period which is more than one minute.

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In this case, the reset actuator may be a mouthpiece cap that, when closed, prevents exposure of the metering chamber to atmosphere.

The inhaler may provide 75 to 125% of labelled claim for a dose following exposure of the metering chamber to atmosphere for a time period which is more than two minutes.

The inhaler may provide 75 to 125% of labelled claim for a dose following exposure of the metering chamber to atmosphere for a time period which is one hour, more than one hour, 24 hours or more than 24 hours.

Operation of the inhaler may include, subsequent to closing the mouthpiece, opening the mouthpiece.

The inhaler may include a metering valve spring and an opposing canister spring for drivingly firing the canister, the metering valve spring, canister spring and metering valve being arranged in the inhaler such that an equilibrium of various forces is achieved in at least one ready-to-fire configuration of the inhaler.

In that case, the operation of the inhaler may include at least one suction force, e.g. provided by a pneumatic chamber; the suction force preferably operating against the canister spring.

In another aspect, the present application discloses use of a metering valve for preventing gas lock within a metering chamber of an inhaler having a pressurised canister, the metering valve having a metering chamber and a valve stem extending from the metering chamber to an interior reservoir of the canister, with the valve stem defining a communication path between the metering chamber and the interior reservoir, the communication path including an opening configured to permit flow between a transfer space inside the valve stem and the interior reservoir, in use the interior reservoir being oriented above the metering chamber so as to cause movement through the opening and gas such as air located within the metering chamber to be replaced with liquid from the interior reservoir.

The use may be performed in a breath actuated inhaler. The inhaler may be oral. Nasal inhalers of this type are also envisaged.

The use may be performed in a metered dose inhaler. The metered dose inhaler may be oral or nasal.

According to a further aspect, the present disclosure discloses an inhaler housing for an inhaler for inhalable substances, the inhaler housing being arranged to contain a pressurised canister for sliding motion within a tubular body portion thereof, the inhaler housing having a valve stem block for connection to a valve stem of a pressurised canister, the valve stem block having a top surface, the tubular body portion having at least two mutually opposed guide ribs for guiding canister position within the tubular body portion, the guide ribs having substantially straight guide edges extending substantially parallel to and spaced from one another, each straight guide edge having an upper corner where the straight guide edge meets a further surface of the rib leading outwardly towards an upper rib section near an inner wall of the tubular body portion, at least one of the ribs having its straight guide edge's upper corner positioned a distance D2 in a direction parallel to an axis of the valve stem block along away from the top surface of the valve stem block, a distance between the straight guide edges of the ribs perpendicular to the axis being ID2, and in which the ratio D2/ID2 is less than 0.8.

It has been surprisingly found that ratios below this value enable very efficient and smooth guidance of the canister relative to the inhaler housing in some configurations.

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The ratio D2/ID2 may be less than 0.75, about 0.7 being one example.

The further surface of at least one guide rib may extend away from the valve stem block and terminate at a distance D3 from the top surface of the valve stem block in the direction parallel to the axis, the ratio D3/ID2 being less than 0.9 or less than 0.85, about 0.8 being one example.

Each guide rib meets the upper rib section near the inner wall of the tubular body portion at outer rib positions wherein the outer rib positions are a distance ID1 apart in a direction perpendicular to the axis, and in which the ratio ID2/ID1 is between 0.7 and 0.9, typically between 0.75 and 0.85, about 0.78 or 0.8 being two examples.

According to a further aspect, the present disclosure discloses an inhaler housing for an inhaler for inhaling inhalable substances, the inhaler having: a body and a dose counter with an actuation member adapted to drive a dose indication portion of the dose counter against a return spring, the body including a recess for location of an end of the return spring; the recess having a substantially flat reaction surface, a shoulder surface adjacent the reaction surface and an entrance mouth into the reaction surface; wherein a distinct guide surface is provided for guiding the end of the return spring into the recess, the distinct guide surface being wider than the entrance mouth in a direction across the mouth.

This feature of the distinct guide surface being wider than the entrance mouth advantageously assists in assembly of the dose counter into the inhaler since when the return spring is being fitted as part of the dose counter installation it can slide along the distinct guide surface relatively easy into the recess.

The entrance mouth may have at least one chamfered entrance lip, the distinct guide surface having a slanted edge which is an extension of the lip.

The distinct guide surface may be substantially planar. The distinct guide surface may have an edge which intersects with an adjacent curved surface of the body.

At least a portion of the distinct guide surface may comprise a portion of the body which is recessed relative to an adjacent portion of the body.

A further aspect of the present disclosure discloses an inhaler housing for an inhaler for inhaling inhalable substances, the inhaler housing having a tubular portion defining a tubular interior space for containing a pressurised canister containing inhaler substances, a valve stem block for engagement with a valve stem of such a pressurised canister, and a dose counter chamber for containing a dose counter assembly, the dose counter chamber being separated from the tubular interior space by a barrier, the barrier including a stepped upper wall area including at least three steps at different levels.

This configuration advantageously permits enough room for the dose counter in the dose counter chamber and enough room for the movable parts inside the inhaler housing including the pressurised canister and in at least one arrangement has been found to be particularly effective in space saving.

The inhaler may include four said steps.

The steps may be arcuate.

The arcuate steps may have substantially flat areas aligned substantially perpendicular to an axis of the valve stem block as well as part-cylindrical riser surfaces between the substantially flat areas.

The steps may be substantially concentric with an axis of the valve stem block.

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The steps may extend around the valve stem block a distance of about 180 degrees.

The material forming the barrier may be of substantially constant thickness substantially throughout the steps.

The dose counter chamber may be formed with at least one heat staking pin for mounting of a dose counter system, the heat staking pin being directly attached to at least two of the steps.

The heat staking pin may be attached to at least one step surface that is oriented substantially perpendicular to an axis of the valve stem block and to at least one and preferably two step risers.

An aperture for a drive pin for actuating the dose counter may be formed through a second furthest step away from the valve stem block.

According to a further aspect, the present disclosure discloses an inhaler valve stem and valve stem block interface for a breath actuated inhaler having a dose counter, a pressurised canister containing inhaler substances including a medicament, which may be in solution or suspension, the valve stem block having a cylindrical inner bore with an inner diameter which is a first diameter, the cylindrical inner bore being for accepting a valve stem with an outer diameter, the valve stem block having a seal in the inner bore with a second diameter which is smaller than the first diameter.

It has been found with this configuration that, surprisingly, better sealing is achieved than with a simple interference fit between a cylindrical outer wall of a valve stem and a cylindrical inner wall of a valve stem block with a larger interference fit. This new configuration has been found to be particularly effective at sealing and avoiding blowback leakage. Especially with regard to the dose counter, the seal permits a relatively low insertion force to be needed to insert the valve stem into the valve stem block and enables very accurate positioning of the valve stem relative to the valve stem block in an axial direction of the valve stem, while at the same time providing a surprisingly effective seal bearing in mind the low insertion force.

The first diameter may be about 3.22 mm.

The first diameter may be about 3.5% larger than the second diameter.

An outer diameter of the valve stem may be smaller than the first diameter but larger than the second diameter prior to introduction of the valve stem into the inner bore, preferably about 0.75% to 1.5% larger, for example about 1% larger.

The valve stem block may include an annular recess concentric with and extending around the inner bore at least partially around the circumference thereof, the inner diameter of the annular recess being about 25 to 50% larger than the inner diameter of the cylindrical inner bore, for example about 40% larger.

The seal may be inwardly convex.

The seal may have an inner surface which is part of a toroid.

The seal may be located at or near an entrance to the inner bore.

The seal may be formed integrally with, e.g. of the same material as, the material defining the inner bore which may, for example, be moulded plastics.

A further aspect of the present disclosure discloses a breath actuated inhaler having a drive adapted to drive a pressurised canister so as to retract a metering valve stem into the canister to fire the canister, the canister being adapted to move during operation between 1 and 4 mm between end positions of its length of travel relative to the valve stem, the drive being arranged to apply a firing force

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of between 15N and 60N of force to the canister at a position of the canister relative to the valve stem at which the canister fires.

With this configuration of drive and canister travel, it has been surprisingly found possible to have very accurate and reliable firing of the canister, as well as accurate counting when a dose counter is provided. Furthermore, a long extent of travel of the canister to retract the valve stem can be provided to ensure that both count and fire very reliably occur.

The drive may comprise a drive spring.

The canister may be arranged to move between 1 and 3 mm between the end positions. In one example the movement between the end positions is 3 mm.

The drive may be adapted to provide the firing force as more than 40N, preferably also less than 60N.

The drive may be adapted to provide the firing force as more than 35N.

The firing force may be greater than the sum at the point of firing of opposing forces applied to the canister by a valve stem spring in the canister and a return spring for an actuator pin of a dose counter of the inhaler.

When the present disclosure is implemented in a metered dose inhaler, this may comprise a press and breathe metered dose inhaler, for example in which a canister is pushed by hand to fire, normally directly although indirect operation is an alternative, normally using finger and/or thumb operation of the canister.

BRIEF DESCRIPTION OF THE DRAWINGS

The present invention may be carried out in various ways and a number of preferred embodiments will now be described by way of example with reference to the accompanying drawings, in which:

FIGS. 1A and 1B show respective isometric views of a preferred inhaler;

FIG. 2 shows an exploded view of the inhaler shown in FIGS. 1A and 1B;

FIG. 3 is an enlarged view of the dose counter assembly shown in FIG. 2;

FIG. 4 is an isometric sectional view of a metering valve of the inhaler and part of the canister shown in FIG. 2;

FIGS. 5A, 5B, 5C and 5D show various details of the inhaler and parts of it in a closed configuration thereof;

FIGS. 6A, 6B, 6C and 6D show various details of the inhaler in an opened configuration thereof;

FIGS. 7A, 7B, 7C and 7D show various details of the inhaler in an actuated configuration thereof;

FIGS. 8A, 8B, 8C and 8D show various details of the inhaler in a closing configuration thereof;

FIG. 9 schematically shows forces and ports within the inhaler in the closed configuration of FIGS. 5A to 5D;

FIG. 10 schematically shows forces and ports within the inhaler in the opened configuration of FIGS. 6A to 6D;

FIG. 11 schematically shows forces and ports within the inhaler in the actuated configuration of FIGS. 7A to 7D;

FIG. 12 is a sectional elevational view of part of the inhaler shown in FIG. 1A with long dash lines denoting the top of ribs used in an earlier prototype;

FIG. 13 shows a portion of the inhaler of FIG. 1A with the dose counter and dose counter door removed;

FIG. 14A is a sectional isometric view of part of the inhaler shown in FIG. 1A;

FIG. 14B shows part of the inhaler with a dose counter not yet installed, showing heat stake pins;

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FIGS. 15A and 15B show respective side elevation and isometric views of the valve stem block of the inhaler of FIG. 1A;

FIGS. 16A, 16B, 17A, 17B, 17C, 17D, 18A, 18B and 18C show various views of part of the inhaler, including components showing the interlocking interaction of the main body of the inhaler with a cap housing thereof;

FIG. 19 shows a modified form of the inhaler of FIG. 1A in which the force holding unit and cap housing are removed and the modified inhaler takes up the form of a metered dose inhaler; and

FIG. 20 shows a side view of the inhaler shown in FIG. 1A; and

FIG. 21 shows a comparative graph of delivered dose recovery at various time delays post previous actuation for the inhaler of FIG. 1A and an inhaler having a metering valve with radial capillary metering chamber inlet and outlet ports.

DETAILED DESCRIPTION OF THE INVENTION

The following detailed description of embodiments of the inhaler and accompanying methods will be better understood when read in conjunction with the appended drawings of exemplary embodiments. It should be understood, however, that the invention is not limited to the precise arrangements and instrumentalities described in the following detailed description.

As shown in FIGS. 1A and 1B, a breath actuated inhaler which is merely an example of an inhaler in accordance with the present invention, includes a force holding unit or cap housing 12, a main body 14, a mouthpiece dust cap 16 and a dose counter door 18 having a dose counter window 20.

As shown by the exploded view of FIG. 2, a dose counter chamber 22 includes a dose counter system 24 closed within it by the dose counter door 18.

The dose counter system is shown in enlarged detail in FIG. 3 and includes an actuating pin 26 and return spring 28. The dose counter can take various forms and may, for example, be as described in EP2135199A or EP2514464A.

As also shown in FIG. 2, the inhaler 10 includes a force holding unit 30 which includes: a filter 32, flap valve housing 34, flap valve 36, flap valve spring 38, main compression spring 40, retaining ring 42, diaphragm 44 and lower cap 46. The inhaler also includes a canister 50 with a metering valve 52 and a valve stem 54; as well as a yoke 56 with drive rods or legs 58 having distal ends 59 which are driven by respective cams 60 on the hingedly-connected mouthpiece dust cap. The valve stem 54 is fitted into an inner bore 61 (FIG. 15B) of a valve stem block 62 which communicates with a nozzle 64 for ejection of inhalable substances through a central bore 68 (FIG. 12) of a mouthpiece 66 (FIG. 12 and FIG. 2) of the main body 14 of the inhaler 10.

The force holding unit 30 operates substantially as disclosed with reference to FIGS. 1 to 3 of EP1289589A and the yoke 56 and mouthpiece dust cap 16 substantially as described in EP2514465A, including but not limited to FIG. 22 thereof.

In particular, with reference to FIGS. 5A to 5D, starting from a configuration in which the mouthpiece dust cap 16 is closed in this configuration the liquid 201 in an interior reservoir 84 of canister 50 communicates with a metering chamber 82 which does not communicate with atmosphere through an interior bore 88 of the valve stem 54. An opening rotation of the mouthpiece dust cap 16 to the configuration

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of FIGS. 6A to 6D enables the distal ends 59 of the drive rods 58 and indeed the whole yoke 56 to be moved away from the cap housing 12 under the influence of the main compression spring 40, the main compression spring 40 being reacted against as equilibrium is reached for the canister position by friction forces as well as forces provided by partial vacuum at the diaphragm, the dose counter return spring 28, and metering valve spring 70 (FIG. 4) which forms part of the metering valve 52. In this configuration, the metering chamber 82 is isolated from both of the interior reservoir 84 and atmosphere.

As the next step, the user (not shown) inhales through the mouthpiece 66 and the drawing out of air through the central bore 68 in turn draws air into the enclosure formed by the main body 14 and cap housing 12 through the series of approximately ten air inlets 72 formed on the cap housing 12. The incoming air impinges upon the flap 74 which releases vacuum (i.e. a partial vacuum) from the vacuum chamber formed by the diaphragm 44 due to flap seal 76 rising off port 78 on diaphragm top plate 80. With the vacuum released, as shown in FIGS. 7A to 7D, as the user is inhaling air through the inhaler 10, i.e. through the apertures 72 and all of the way along inside the cap housing 12 and main body 14 past the canister 50 and out through the central bore 68, the main compression spring 40 drives the lower cap 46, yoke 56 and canister 50 away from the cap housing 12 and towards the main body 14 and valve stem block 62 whereby the valve stem 54 is retracted into the canister 50. This places the pressurised metering chamber 82 in communication with valve stem block nozzle 64 so fires the canister and ejects inhalable substances from the metering chamber 82 through the nozzle 64 and mouthpiece 66 towards the lungs (not shown) of the user. The dose counter system 24 also registers a count by movement of the actuating pin 26 by the canister ferrule 220. At this time after opening and firing, the metering chamber 82 communicates with atmosphere. With the mouthpiece 66 left open such that the atmosphere communicates through the bore 88 and exit port 90 with the metering chamber 82, the metering chamber 82 can become at least partially or fully filled with gas such as air from the atmosphere.

In other embodiments comprising nasal inhalers, the mouthpiece 66 may be replaced with a nose piece.

As shown in FIGS. 8A to 8D, during closing, the mouthpiece dust cap 16 is rotated back to its closed position and the cams 60 push on the distal ends 59 of the drive rods 58 so as to push the yoke 56 towards the cap housing 12 so as to compress the main compression spring 40 again and the vacuum is formed again at the diaphragm 44. At the same time, the canister is pushed back to its original configuration of FIGS. 5A to 5D by the metering valve return spring 70.

As shown in FIG. 9, with the inhaler 10 in the configuration of FIGS. 5A to 5D, the metering valve spring 70 keeps the valve stem 54 extended, the inlet port 86 open and the exit port 90 effectively closed, i.e. with the metering chamber 82 isolated from atmosphere. At the same time the force F_{YL} applied as $F_{YL}/2$ by each of the legs or rods 58 of the yoke 56 to the lower cap 46 is greater than or equal to the force F_{FHUCS} applied in the opposite direction by the spring of the force holding unit 12.

As shown in FIG. 10, with the inhaler then changed to the configuration of FIGS. 6A to 6D, the canister is displaced to a representative distance D_{valve} from the canister position of FIG. 9 where this displacement at D_{valve} is less than the displacement required to actuate and fire a dose. In this FIG.

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10 configuration, the position of the canister 50 is determined by an equilibrium between forces, which is:

$$F_{\text{valve CS}} + F_{\text{Dia}} = F_{\text{FHU CS}}$$

where $F_{\text{valve CS}}$ is the force applied to the canister by the metering valve spring 70, F_{Dia} is the force applied by the partial vacuum in the diaphragm 44 in the same direction and $F_{\text{FHU CS}}$ is the opposing force applied by the compression spring 40 of the force holding unit 30. The port 78 is noted to be closed. The port 86 is open and the port 90 is closed.

As the user then inhales, the port 78 is opened by the action of air entering through the apertures 72 impinging on the flap 74, lifting flap seal 76. The equilibrium of FIG. 10 is therefore lost. The canister 50 is therefore moved to displace the valve stem 54 more, to the configuration of FIG. 11, so that the canister is a representative distance D_{Actuated} from the valve stem block 62, and where the force balance is that $F_{\text{valve CS}} \leq F_{\text{FHU CS}}$ in which the force applied to the lower cap 46 is less than or equal to the opposing force applied by the compression spring 40 of the force holding unit R. In this configuration, the port 86 has closed to isolate the metering chamber 82 from the interior reservoir 84 of the canister 50 and after this closure the port 90 has opened, thereby firing the canister 50 by venting pressurised contents within the metering chamber 82 out through the nozzle 64 of the valve stem block 62 for inhalation by the user.

The spring 40 is adapted such that the firing force $F_{\text{FHU CS}}$ is more than 35 N, typically less than 60 N. This may vary in other embodiments.

In most embodiments, the spring 40 is adapted in addition to device geometry such that the force exerted by the spring 40 on the valve/canister is equal to the sum of the opposing valve spring 70 and pneumatic resistance force in the FHU diaphragm 44 in the prepared position. Nonetheless, the spring 40, unless otherwise assisted, must be able to provide sufficient force once the mechanism is triggered to actuate the canister on inhalation. The specific force values will be dependent on the componentry of the device, driven predominantly by the force required to actuate the canister at a specific displacement, thus the spring 40 will be adapted to suit.

The metering valve 52 shown in FIG. 4 is similar to those described in U.S. Pat. No. 7,959,042B, which is incorporated by reference herein, and has the metering chamber 82 arranged for selective communication with either the interior reservoir 84 of the canister 50 via an inlet port 86, or with the interior bore 88 (FIGS. 5A to 5D) of the valve stem 54 which communicates via the valve stem block 62 with the nozzle 64, the valve stem 54 being provided with a radially configured capillary exit port 90 leading to the bore 88. The metering chamber 82 is at least partly defined by a cup-shaped inner metering body 92 and has an inner seal 94 and outer seal 96, as well as a location member 98, a main canister seal 100 and a crenelated valve stem driver 102 which has a through bore 104 axially directed towards the inlet port 86. The inlet port 86 includes two elongate openings 106 diametrically opposed to one another and which are defined by a pair of forked legs 108 which are spaced apart from one another by the elongated openings 106 and the open space forming the inlet port 86 between them. The forked legs 108 have substantially constant cross-section all the way along to their distal ends (not shown) which are located within the crenelated valve stem driver 102.

When the valve stem 54 is depressed into the canister 50 so that the inlet port 86 permits communication between the

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metering chamber 82 and the interior reservoir 84, the communication into the interior reservoir 84 is at an inner side 110 of the inner seal 94 and it will be appreciated that this is a slot-shaped porting between the forked legs 108 from where flow can travel directly axially into or out of the interior reservoir 84.

According to an alternative embodiment, the arrangement of openings in the metering valve of the present invention is similar to those described in US2016/0084385, which is incorporated by reference herein. In particular, the metering valve of the present invention may be similar to the embodiment shown in FIG. 4 of US2016/0084385, in which the valve body includes at least one first opening (i.e., at least one first side hole 100 that is arranged in a cylindrical portion of the valve body) and at least one second opening (i.e., at least one second hole 111 that, as with the first hole(s), is arranged in a cylindrical portion of the valve body), the second opening(s) being axially offset relative to the first opening(s) along a longitudinal axis that extends between a first axial end and a second axial end of the valve body. The first opening(s) and second opening(s) that are axially offset from each other along the valve body enable the metering chamber to be filled and emptied.

The canister 50 includes inhalable substances including the active ingredient beclomethasone dipropionate and the propellant HFA134a which has a surface tension of about 8 mN/m as liquid at 25° C. Other active ingredients may be used in other embodiments, such as tiotropium bromide.

If the mouthpiece dust cap 16 is left open such that the atmosphere communicates through the bore 88 and exit port 90 with the metering chamber 82, the metering chamber can become at least partly or substantially fully filled with gas such as air from the atmosphere. When the mouthpiece dust cap 16 is closed, however, and when the interior reservoir 84 is oriented above the metering chamber 82, the present inventors have discovered that the liquid phase in the interior chamber can exchange places with gas in the metering chamber 82, the fluid travelling either directly through the openings 106 or through the throughbore 104, and along through the inner seal 94 and into the metering chamber 82 and gas in the metering chamber 82 can travel in the reverse direction along the same path, exiting with an axial component through between the forked legs 108 and through the elongated openings 106 into the interior reservoir 84. It is believed that the particular surface tension of the chosen propellant promotes this action and the higher density of the liquid than that of any gas in the metering chamber enabling the latter to rise up in and relative to the liquid.

The full filling of the metering chamber 82 with a dose of liquid from the interior reservoir 84 with any gas in the metering chamber passing in the reverse direction from the metering chamber 82 into the interior reservoir 84 is highly advantageous since with this one extension of the valve stem 54 from its retracted configuration after inhalation to its extended configuration with the mouthpiece dust cap 16 closed again ensures that the inhaler 10 is fully primed for use. This has overcome a significant problem.

As shown in FIG. 20, the inhaler 10 may be provided with a preventer 110 for preventing the user from taking a second or further inhalation while the dust cap 16 is still open. The preventer 110 may take the form of a warning signaler 102 such as a warning notice as shown in the drawing stating "to reload: close before each inhalation" although in other embodiments the preventer 110 could take various other forms such as an alarm or audible or visual warning device to indicate that the mouthpiece dust cap 16 is open and needs to be closed prior to the next inhalation.

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FIG. 21 is a graph showing a comparison of the inhaler of FIG. 1A with delivered dose for a prior art breath actuated inhaler with a different metering valve (not shown) in which the exit port from the interior reservoir comprises a radially oriented capillary bore which leads to an internal bore of the valve stem leading axially towards a further radially extending capillary port, such that the communication from the interior space is through the first capillary port, along the internal bore and out through the second radial capillary port into the metering chamber when the valve stem is in its extended configuration. In all cases the inhalers were held with the valve stems vertical and the canister interior reservoir above the metering chamber. After inhalation, the valve stem in each case was left in the retracted inhale configuration with the metering chamber exposed to atmosphere through the valve stem for the specified delay period and the inhaler was then reset and readied for inhalation, in the case of the present inhaler 10 by closing and opening the mouthpiece cap again. As shown by the graph of FIG. 21, with a target of 80 micrograms of BDP (beclomethasone dipropionate) the diamond shaped plots 205 are for the prior art inhaler which began to fail to reach 75% of the labelled claim for the dose after a delay of 30 seconds after inhalation in closing the mouthpiece cap to isolate the metering chamber from atmosphere. At all delays of 2 minutes or over, the prior inhaler failed to provide 75% of the labelled claim of dose in 100% of cases. This, the present inventors have discovered, is due to gas lock forming in the metering chamber after inhalation due to the metering chamber's exposure to atmosphere, i.e. in that when the mouthpiece cap is closed after a delay air is trapped in the metering chamber and is not replaced by liquid in the interior reservoir even when the metering chamber is connected to the interior reservoir. In contrast, the plots of crosses 207 in FIG. 21 show the performance of the inhaler of FIG. 1A. Here, 100% of the plots are in the range of 75 to 125% of labelled claim for the dose, even when there is no appreciable delay or a delay of one hour, twelve or twenty-four hours before closing the mouthpiece cap after inhalation.

Therefore, even if the metering chamber 82 has been exposed to atmosphere for a relatively long time such that it is after that delay substantially full of gas due to evaporation/diffusion of substances after inhalation, this graph clearly shows that by closing the mouthpiece fully and opening it again, the gas in the metering chamber 82 is removed into the interior reservoir 84 and replaced with a correct dose very reliably.

Although FIG. 21 data is presented for 80 mcg (ex-actuator) targeted BDP HFA product, the data is representative of any formulation and formulation strength.

As shown in FIG. 12, the main body 14 has a tubular body portion 120 arranged to contain the pressurised canister 50 for sliding motion. As shown in FIG. 12, the valve stem block has a top surface 122 and the tubular body portion 120 has at least two mutually opposed guide ribs 124, 126. The guide ribs 124, 126 have substantially straight guide edges 130, 132 extending parallel to and spaced from one another, each straight guide edge 130, 132 having an upper corner 134, 136 where the straight guide edge meets a further surface 138, 140 of the ribs 124, 126 leading outwardly towards an upper rib section near an inner wall 146 of the tubular body portion 120. At least one of the ribs 124, 126 has its straight guide edge's upper corner 134, 136 positioned a distance D2 in a direction parallel to an axis of the valve stem block 62 along away from the top surface 122 of the valve stem block 62, a distance between the straight guide edges 130, 132 of the ribs 124, 126 perpendicular to

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the axis being ID2, and the ratio D2 divided by ID2 is 0.7. This is smaller than in previous embodiments and can surprisingly assist in providing smooth guiding of the canister within the tubular body portion 120.

The further surface 138, 140 of at least one of the guide ribs 124, 126 and in this case both of them extends away from the valve stem block 62 and terminates at a distance D3—in the case of guide rib 124—from the top surface 122 of the valve stem block 62 in the direction parallel to the axis, the ratio D3 divided by ID2 being 0.8, the equivalent ratio for the guide rib 126 being 1.0. Each guide rib meets the upper rib section 142, 144 near the inner wall 146 of the tubular body portion 120 at an outer rib position 148, 150 wherein the outer rib positions are a distance apart ID1 in a direction perpendicular to the axis 202 of the valve stem block 62 and the ratio ID2 divided by ID1 is 0.8. This arrangement assists beneficially in providing sufficient space for the canister 50 to move within the tubular body section 120.

With reference to FIG. 13, a portion of the main body 16 is shown with the mouthpiece dust cap 16 and the dose counter door 18 and the dose counter system 24 not yet installed. As can be seen, the dose counter chamber 22 includes a recess 152 for location of an end 154 (FIG. 3) of the return spring 28. The recess 152 has a substantially flat reaction surface for pushing on the end 154 of the return spring 28. The recess 152 also has a shoulder surface 158 adjacent the reaction surface 156 and an entrance mouth 160 into the reaction surface 156. A distinct guide surface 162, which is substantially planar is provided for guiding the end 154 of the return spring 28 into the recess 152 during assembly. The distinct guide surface 162 is wider than the entrance mouth 160 in a direction across the mouth and this assists substantially in assembling the spring 28 into the recess 152.

The entrance mouth 160 also has at least a chamfered entrance lip 164, an extension 166 of which into the guide surface forms a slanted edge 166 of the distinct guide surface 162. At least a portion of the distinct guide surface 162 comprises a portion of the body 14 which is recessed relative to the adjacent and partially surrounding portion 164 of the body by an edge 168. The edge 168 is particularly effective in catching the end 154 of the return spring and the wide guide surface 162 is effective in guiding the spring 28 past the chamfered entrance lip 164 and onto the reaction surface 156 where it remains once installed. A further edge 170 of the guide surface 162 is spaced from and generally parallel to the edge 168. The edge 170 forms an intersection with an adjacent portion 171 of the body 14.

As shown in FIG. 14A, the main body of the inhaler 10 includes a barrier 180 separating an interior space 182 defined at least partly by the tubular body portion 120 from the dose counter chamber 22. The barrier includes a stepped upper wall area 184 which has four steps 186, 188, 190, 192 at different levels. The steps are arcuate and have substantially flat parts 194, 196, 198, 200 aligned substantially perpendicular to the axis 202 of the valve stem block as well as a part-cylindrical risers 204, 206, 208 between the substantially flat parts 194, 196, 198, 200.

The arcuate steps 186, 188, 190, 192 are substantially concentric with the axis 202 of the valve stem block 62. The steps 186, 188, 190, 192 extend around the valve block 62 a distance/angle of about 170° although this is only approximate and may be in the region of about 180 to 120° in various embodiments. The material forming the barrier 180

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is of substantially constant thickness throughout the steps **186, 188, 190, 192** which is advantageous for manufacturing techniques by moulding.

As shown in FIG. **14B** which is a view into the dose counter chamber **22**, the dose counter chamber **22** is formed with two heat staking pins **212, 214** for attaching the dose counter system **24** permanently into position within the dose counter chamber **22**. One of the heat staking pins **214** is directly attached to two of the steps **188, 190**. The heat staking pin **214** is attached to one substantially flat step part **198** and to two step risers **206, 208**, providing secure and advantageous location of the heat staking pin **214** in the stepped upper wall area **184** of the barrier **180**. An aperture **218** for the actuating pin **26** of the dose counter system **24** is formed through the second furthest step part **198** away from the valve stem block **62**.

The stepped upper wall area **184** is highly advantageous since it enables the accommodation of a length of movement of the canister **50** and in particular its ferrule **220** (FIG. **2**) within the main body **14**. Therefore, even with a metering valve **70** as used in the inhaler **10** which has a relatively long end-to-end travel of approximately 4 mm, the internal components can be maintained within a relatively small and compact inhaler **10**, while also allowing for space in the dose counter chamber **22** for the dose counter system **24** and enabling the dose counter to be heat staked firmly in place by the heat stake pins **212, 214** including the pin **214** which is attached to the stepped upper wall area **84** of the barrier **180**.

As shown in FIGS. **15A** and **15B**, the valve stem block **62** has the cylindrical inner bore **61** which has an inner diameter **B1** which has a first diameter, a seal **224** at an entrance to the inner bore **61** having a second diameter **BD2** which is smaller than the first diameter. The seal **224** is inwardly convex and/or is toroidal. The first diameter **B1** is about 3.22 mm and is about 3.5% larger than the second diameter **BD2**. The valve system **54** has a cylindrical outer surface **226** (FIG. **2**) with a diameter which is smaller than the first diameter **BD1** but larger than the second diameter **BD2** prior to introduction of the valve stem **54** into the inner bore **61** and is about 1% larger. The valve stem block **62** also includes an annular recess **228** which extends more than half way around the periphery of the inner bore **61**, in this embodiment about 350° or more. The annular recess **228** has an inner diameter which is about 40% larger than the inner diameter **B1** of the cylindrical inner bore **61**. This arrangement has been found to provide extremely effective sealing against blowback which has occurred in prior designs which have a substantially greater interference fit between the exterior diameter of the valve stem and the interior diameter of the inner bore of the valve stem. Surprisingly, and advantageously, using the inwardly convex seal **224** to the bore **61**, very effective sealing without any blowback can be achieved even with a relatively small interference fit between the valve stem **54** and the seal **224**, the annular recess **228** assisting in providing resilience to the valve stem block **62** for this purpose. The small interference fit allows for good sealing even when the inhaler **10** is subjected to high temperatures for long periods since there is little stress to relieve. Furthermore, the seal **224** permits a relatively low insertion force for inserting the valve stem **54** into the valve stem block **62** and this enables accurate positioning of these two components relative to one another in an axial direction of the valve stem **54** so that the dose counter system **24** can count reliably by way of accurate actuation of its actuator pin **26** by the canister ferrule **220**.

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A coupling element may couple the cap housing **12** to the main body **14**. As shown in the various sectional views of FIGS. **16A** through to **18C**, a lock system **250** is provided for locking the cap housing or force holding unit housing **12** on the main body **14**. The lock system **250** may be a bi-directional lock system. Helical threads **252, 254** are provided, with male threads **252** on the cap housing **12** and female threads **254** on the main body **14**, for rotational attachment of the cap housing **12** on the main body **14** and for resisting relative longitudinal movement therebetween without rotation.

The lock system **250** includes a protrusion **256** in the region of the helical thread **254** on the main body **14** which is lockable in a recess **258** in the region of the helical thread **252** on the cap housing. As shown in FIG. **17C**, the inhaler **10** includes two of the protrusions **256** in two of the recesses **258** formed at opposing locations on the inhaler, i.e. diametrically opposite to one another. As shown in FIG. **18A**, each protrusion **256** has a leading ramp surface **260** and a trailing ramp surface **266**, the included angle **A** between the ramp and trailing surfaces **260, 266** being 115°, although a range of about 95 to 120° is envisaged. The recesses have a similar included angle which is smaller than the angle of the protrusion **256** at about 100°. This ensures that the protrusion **256** will fit securely in the recess **258** without any play rotationally.

The main body **14** has a central axis **202** coincident with that **202** of the valve stem block **62** and the ramp surfaces **266** are inclined at an angle of about 45°±15° to tangential.

The lock system **250** also includes a first lock member **270** on the cap housing **12** which is adapted to engage a second lock member **272** at a lock interface **274** formed by respective engagement faces thereof, the lock interface **274** being oriented substantially perpendicular to tangential. This therefore assists in preventing rotation. The first lock member **270** has a radial extent of 0.39 mm, although about 0.35 to 0.45 mm is envisaged in other embodiments or 0.25 to 0.75 mm. The second lock member **272**, it will be appreciated, has a greater radial extent. The first lock member **270** has a longitudinal extent parallel to the axis **202** of about 10 mm.

The main body **14** and cap housing **12** are formed of plastics material and the lock system **250** is configured so that a release torque required to overcome the locking provided by the plastics main body and cap housing at the lock interface **274** and at the protrusions **256** and recesses **258** is more than 1 Nm. In the described example, the release torque is about 2.75 Nm. When an information sticker is applied over the top of the interface between the main body **14** and cap housing **12** the release torque may rise to about 3.5 Nm. This has been found to be lower than 4 Nm and this is low enough that a laboratory is capable of opening up the inhaler **10** for inspection without significant destruction. However, this level of torque is significantly higher than likely to be tried by a user in an attempt to open the inhaler **10** which might result in tampering and damage to the components of the inhaler **10**.

In an alternative design, the radial extent of the first locking member **270** is significantly greater at about 0.73 mm and this has been found, surprisingly, to provide a removal torque which is considered too high at 4.6 Nm for laboratory disassembly without destruction. In contrast, a design omitting the first lock member **270** was found to provide a removal torque of only 0.7 Nm which is considerably too low and likely to result in users rotating the cap housing **12** off the main body **14** and potentially damaging the inhaler by investigating the contents. In fact, this was the

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first design attempted by the present inventors and the next step was to double up the number of protrusions **256** and recesses **258** so that there are four in total in an attempt to double the torque, at least, from 0.7 Nm. However, surprisingly, with this design, the removal torque was only increased by about 10% to 0.8 Nm. The ideal remove torque was surprisingly achieved with only one protrusion **256** on each thread **254** and with a locking member **270** with only a small radial extent of 0.39 mm. The locking member **270** advantageously also includes a lead ramp **290** for achieving a smooth snap lock of the cap housing **12** onto the main body **14** when the cap housing **12** is twisted into the locked position.

FIG. **19** shows a modification of the inhaler **10** to form an inhaler **1000** which is a metered dose inhaler having a main body **1002** and mouthpiece dust cap **1004** for the mouthpiece **1006** for stopping foreign objects entering the central bore **1008** of the mouthpiece **1006** and for protecting the mouthpiece generally. This metered dose inhaler **1000** does not include the cap housing **12** or the force holding unit **30** or yoke **56** but it does include the same dose counter chamber **22**, dose counter system **24**, canister **50** and metering valve **52** and valve stem **54** and valve stem block **62** as that in the inhaler **10**. If this metered dose inhaler is left with the canister **50** accidentally depressed, for example while squashed in luggage or clothing by mistake, such that the metering chamber is left exposed to the atmosphere for a considerable period of time, then when the inhaler **1000** is located and turned upright for use with respective gravity with the canister allowed to extend to its rest position in which the metering chamber communicates with the interior reservoir, any gas such as air which has entered the metering chamber is easily expelled up into the interior reservoir of the canister just as in the inhaler **10** such that an accurate next dose is applied and the problem of gas lock is therefore avoided.

Inhalers in accordance with preferred embodiments of the present invention are suitable for the delivery of many classes of active ingredients by inhalation, and may be used for the treatment of various diseases and disorders. According to preferred embodiments, the inhaler is used for the treatment of respiratory disorders (e.g., COPD, asthma and/or cystic fibrosis). The inhaler may also be used to treat non-respiratory disorders, such as migraine. According to an embodiment, a method of treating a respiratory disease or disorder comprises actuating the inhaler to administer a therapeutically effective amount of one or more active ingredients. As described herein, the canister of the inhaler contains a drug formulation comprising one or more active ingredients in suspension or in solution. Preferably, the drug formulation comprises one or more active ingredients in propellant (e.g., HFA). The drug formulation may optionally comprise one or more excipients in combination with the active ingredient(s) and propellant.

In certain embodiments, the inhaler described herein can be used to treat patients suffering from a disease or disorder selected from asthma, chronic obstructive pulmonary disease (COPD), exacerbation of airways hyper reactivity consequent to other drug therapy, allergic rhinitis, sinusitis, pulmonary vasoconstriction, inflammation, allergies, impeded respiration, respiratory distress syndrome, pulmonary hypertension, pulmonary vasoconstriction, and any other respiratory disease, condition, trait, genotype or phenotype that can respond to the administration of, for example, a long-acting muscaric antagonist (LAMA), long-acting β 2-adrenergic agonist (LABA), corticosteroid, or other active agent as described herein, whether alone or in

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combination with other therapies. In certain embodiments, the compositions, systems and methods described herein can be used to treat pulmonary inflammation and obstruction associated with cystic fibrosis. As used herein, the terms “COPD” and “chronic obstructive pulmonary disease” may encompass chronic obstructive lung disease (COLD), chronic obstructive airway disease (COAD), chronic airflow limitation (CAL) and chronic obstructive respiratory disease (CORD) and include chronic bronchitis, bronchiectasis, and emphysema. As used herein, the term “asthma” refers to asthma of whatever type or genesis, including intrinsic (non-allergic) asthma and extrinsic (allergic) asthma, mild asthma, moderate asthma, severe asthma, bronchitic asthma, exercise-induced asthma, occupational asthma and asthma induced following bacterial infection. Asthma is also to be understood as embracing wheezy-infant syndrome.

A range of classes of active ingredients have been developed to treat respiratory disorders and each class has differing targets and effects.

Bronchodilators are employed to dilate the bronchi and bronchioles, decreasing resistance in the airways, thereby increasing the airflow to the lungs. Bronchodilators may be short-acting or long-acting. Typically, short-acting bronchodilators provide a rapid relief from acute bronchoconstriction, whereas long-acting bronchodilators help control and prevent longer-term symptoms.

Different classes of bronchodilators target different receptors in the airways. Two commonly used classes are anticholinergics and β 2-agonists.

Anticholinergics (or “antimuscarinics”) block the neurotransmitter acetylcholine by selectively blocking its receptor in nerve cells. On topical application, anticholinergics act predominantly on the M3 muscarinic receptors located in the airways to produce smooth muscle relaxation, thus producing a bronchodilatory effect. Non-limiting examples of long-acting muscarinic antagonists (LAMA’s) include tiotropium (bromide), oxitropium (bromide), aclidinium (bromide), ipratropium (bromide) glycopyrronium (bromide), oxybutynin (hydrochloride or hydrobromide), tolterodine (tartrate), trospium (chloride), solifenacin (succinate), fesoterodine (fumarate), darifenacin (hydrobromide) and umeclidinium (bromide). In each case, particularly preferred salt/ester forms are indicated in parentheses.

β 2-Adrenergic agonists (or “ β 2-agonists”) act upon the β 2-adrenoceptors and induce smooth muscle relaxation, resulting in dilation of the bronchial passages. Non-limiting examples of long-acting β 2-adrenergic agonists (LABA’s) include formoterol (fumarate), salmeterol (xinafoate), indacaterol (maleate), bambuterol (hydrochloride), clenbuterol (hydrochloride), olodaterol (hydrochloride), carmoterol (hydrochloride), tulobuterol (hydrochloride) and vilanterol (triphenylacetate). Non-limiting examples of short-acting β 2-agonists (SABA’s) include albuterol (sulfate) and levalbuterol (tartrate). In each case, particularly preferred salt/ester forms are indicated in parentheses.

According to one embodiment, the formulation comprises albuterol (sulfate).

Another class of active ingredients employed in the treatment of respiratory disorders are inhaled corticosteroids (ICS’s). ICS’s are steroid hormones used in the long-term control of respiratory disorders. They function by reducing the airway inflammation. Non-limiting examples of inhaled corticosteroids include budesonide, beclomethasone (dipropionate), fluticasone (propionate), mometasone (furoate), ciclesonide and dexamethasone (sodium).

According to one embodiment, the formulation comprises beclomethasone dipropionate.

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According to an embodiment, the inhaler delivers one or more active ingredients selected from the group consisting of tiotropium (bromide), oxitropium (bromide), acclidinium (bromide), ipratropium (bromide) glycopyrronium (bromide), oxybutynin (hydrochloride or hydrobromide), tolterodine (tartrate), trospium (chloride), solifenacin (succinate), fesoterodine (fumarate), darifenacin (hydrobromide), umeclidinium (bromide), formoterol (fumarate), salmeterol (xinafoate), indacaterol (maleate), bambuterol (hydrochloride), clenbuterol (hydrochloride), olodaterol (hydrochloride), carmoterol (hydrochloride), tulobuterol (hydrochloride), vilanterol (triphenylacetate), albuterol (sulfate), levalbuterol (tartrate), budesonide, beclomethasone (dipropionate), fluticasone (propionate), mometasone (furoate), ciclesonide, dexamethasone (sodium) and a combination thereof.

According to particular embodiments, the inhaler delivers a combination of at least two different active ingredients (two, three, four, etc.) which belong to the same or different classes. According to one embodiment, the inhaler delivers a "triple combination" of three different active ingredients. The three active ingredients may belong to three different active ingredient classes (e.g., LAMA, LABA, ICS); alternatively, two or three of the active ingredients may belong to the same class.

According to additional embodiments, the inhaler delivers one or more active ingredients selected from the group consisting of a long-acting muscarinic antagonist (LAMA), a long-acting β 2-adrenergic agonist (LABA), an inhaled corticosteroid (ICS) and a combination thereof. Thus, the inhaler may deliver a formulation comprising one or more LAMA's, one or more LABA's and one or more ICS's. That is, the device may deliver a double combination of a LAMA and a LABA, a LAMA and an ICS, or a LABA and an ICS; or a triple combination of a LAMA, a LABA and an ICS.

According to an alternative embodiment, the inhaler delivers one or more active ingredients for the treatment of a headache disorder, such as migraine. For example, the inhaler may deliver dihydroergotamine (DHE) or a pharmaceutically acceptable salt thereof, such as dihydroergotamine mesylate.

In one embodiment the inhaler comprises a reservoir, particularly a pressurized canister, comprising an active ingredient.

Preferably the active ingredient is presented in a pharmaceutical formulation comprising a propellant, optionally a co-solvent and optionally other pharmaceutically acceptable excipients.

Preferred propellants include hydrofluoroalkanes, in particular 1,1,1,2-tetrafluoroethane (HFA134a), 1,1,1,2,3,3,3-heptafluoropropane (HFA227), or combinations thereof. Most particular propellant is HFA134a. Most particular HFA134a concentration is from about 91.8% w/w to 92.9% w/w.

HFA134a has a low boiling point ($-26.1^{\circ}\text{C}.$) and correspondingly high vapor pressure (572 kpa) at $20^{\circ}\text{C}.$

Particular co-solvents are selected from the list of aliphatic alcohols (particularly ethanol), glycerols and glycols. Most particular co-solvent is ethanol. Most particular ethanol concentration is about 8% w/w.

Ethanol is well known to be compatible with HFA-134a and increases the solubility of BDP. Ethanol (anhydrous) is used as a co-solvent to aid solubility of BDP in HFA134a. A concentration of around 8% w/w of ethanol is known to provide necessary stability, preventing precipitation and achieving correct aerosol performance.

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Other pharmaceutically acceptable excipients include surfactants, particularly oleic acid.

Preferably, the active ingredient is suspended in the propellant. Alternatively the active ingredient is dissolved in the propellant. The active ingredient may also be partly suspended and partly dissolved in the propellant.

A particular active ingredient is selected from the group consisting of anti-inflammatory agents, β 2-adrenoreceptor agonists, anti-cholinergic agents, anti-histamines, serotonin agonists, and combinations thereof.

A particular corticosteroid is beclomethasone dipropionate (BDP).

A particular β 2-adrenoreceptor agonist is salbutamol sulphate.

In a particular embodiment of the invention, the active ingredient is selected from beclomethasone dipropionate (BDP), salbutamol sulphate and dihydroergotamine.

In a particular embodiment the inhaler comprises a pressurized canister comprising beclomethasone dipropionate as active ingredient, HFA134a as propellant and ethanol as co-solvent.

In a particular embodiment the inhaler comprises a pressurized canister comprising beclomethasone dipropionate as active ingredient at about 1.0 mg/ml, HFA134a as propellant at about 1090.20 mg/ml and ethanol as co-solvent at about 94.80 mg/ml.

In a particular embodiment the inhaler comprises a pressurized canister comprising beclomethasone dipropionate as active ingredient at about 0.084% w/w, HFA134a as propellant at about 91.9% w/w and ethanol as co-solvent at about 8.0% w/w.

In a particular embodiment the inhaler comprises a pressurized canister comprising beclomethasone dipropionate as active ingredient at about 0.169% w/w, HFA134a as propellant at about 91.8% w/w and ethanol as co-solvent at about 8.0% w/w.

In a particular embodiment the inhaler comprises a pressurized canister comprising salbutamol sulphate as active ingredient, HFA134a as propellant and ethanol as co-solvent.

In a particular embodiment the inhaler comprises a pressurized canister comprising about 0.1098 mg of salbutamol sulphate as active ingredient, about 27.8 mg of HFA134a as propellant and about 3.6 mg of ethanol as co-solvent.

One embodiment relates to an inhaler as described herein comprising an active ingredient.

One embodiment relates to an inhaler as described herein comprising an active ingredient for therapeutic use.

One embodiment relates to an inhaler as described herein comprising an active ingredient for use in the treatment or prevention of a respiratory disease, particularly COPD or Asthma.

One embodiment relates to an active ingredient for use in the treatment or prevention of a respiratory disease, particularly COPD or Asthma, wherein the active ingredient is delivered to a patient using an inhaler as described herein.

One embodiment relates to a method for the treatment or prevention of respiratory diseases, particularly COPD or Asthma, which method comprises administering an active ingredient to a human being or animal using an inhaler as described herein.

One embodiment relates to the use of an inhaler as described herein comprising an active ingredient for the treatment or prevention of respiratory diseases, particularly COPD or Asthma.

Embodiments of the present invention may be further understood by reference to the Example provided below.

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Example

According to the following example, a method of using the inhaler of the present invention comprises delivering a therapeutically effective amount of beclomethasone dipropionate HFA for the treatment of asthma, particularly for the maintenance treatment of asthma as prophylactic therapy in patients 4 years of age and older, wherein the inhaler is a breath-actuated inhaler (BAI) as described herein and the step of actuating the inhaler comprises inhaling through the inhaler. The breath-actuated inhaler may be used by patients to deliver at least about 40 mcg beclomethasone dipropionate upon each actuation, preferably twice daily, e.g., it may be used by patients 4 to 11 years old to deliver 40 mcg or 80 mcg beclomethasone dipropionate twice daily, or may be used by patients 12 years of age and older to deliver 40 mcg, 80 mcg, 160 mcg or 320 mcg beclomethasone dipropionate twice daily. Actuation of the breath-actuated inhaler is preferably triggered by an inspiratory flow rate of at least about 20 liters per minute (L/min), and includes a primeless valve so that no priming actuations are required before use. A method of treating asthma may comprise inhaling through the BAI at a flow rate of at least about 20 L/min without priming the inhaler before use, wherein the inhaler comprises a primeless valve as described herein and wherein the mean change from baseline for FEV₁ between 2-6 weeks or between 2-12 weeks or between 4-12 weeks of using the BAI is greater than about 0.150 L or greater than about 0.200 L. Preferably, the mean peak plasma concentration (C_{max}) of BDP is between about 6000 pg/mL and about 7000 pg/mL or between about 6200 pg/mL and about 6800 pg/mL at 2 minutes after inhalation of 320 mcg using the BAI (4 inhalations of the 80 mcg/inhalation strength). The mean peak plasma concentration of the metabolite 17-BMP is preferably between about 1000 pg/mL and about 2000 pg/mL or between about 1200 pg/mL and about 1700 pg/mL at 10 minutes after inhalation of 320 mcg of the BAI.

The breath-actuated inhaler (BAI) in this example included a canister having an interior reservoir containing pressurised inhalable substances including fluid; a “primeless” metering valve including a metering chamber and a valve stem defining a communication path between the metering chamber and the interior reservoir, the communication path including an opening configured to permit flow between a transfer space inside the valve stem and the interior reservoir, the interior reservoir being arranged for orientation above the metering chamber whereby gas such as air located within the metering chamber is replaced with liquid from the interior reservoir. Preferably, the primeless metering valve is the embodiment shown in FIG. 4 and described in U.S. Pat. No. 7,959,042B. Alternatively, the primeless metering valve is similar to the embodiment shown in FIG. 4 of US2016/0084385, as described herein.

Two confirmatory Phase 3 clinical trials were conducted comparing the above-described breath-actuated inhaler with placebo in adult and adolescent patients with persistent asthma (Trial 1 and Trial 2).

Trial 1: This randomized, double-blind, parallel-group, placebo-controlled, 12-week, efficacy and safety trial compared the breath-actuated inhaler 40 and 80 mcg given as 1 inhalation twice daily with placebo in adult and adolescent patients with persistent symptomatic asthma despite low-dose inhaled corticosteroid or non-corticosteroid asthma therapy. Patients aged 12 years and older who met the entry criteria including FEV₁ 40-85 percent of predicted normal, reversible bronchoconstriction of 15% with short-acting inhaled beta-agonist entered a 14-21 day run-in period. 270

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patients (104 previously treated with inhaled corticosteroids) who met all the randomization criteria including asthma symptoms and rescue medication use were discontinued from asthma maintenance medication and randomized equally to treatment with the breath-actuated inhaler (BAI) 80 mcg/day BDP, the breath-actuated inhaler 160 mcg/day BDP or placebo. Baseline FEV₁ values were similar across treatments. The primary endpoint for this trial was the standardized baseline-adjusted trough morning forced expiratory volume in 1 second (FEV₁) area under the effect curve from time zero to 12 weeks [FEV₁ AUEC(0-12wk)]. Patients in both treatment groups had significantly greater improvements in trough FEV₁ compared to placebo (BAI 80 mcg/day, LS mean change of 0.124 L and BAI 160 mcg/day, LS mean change of 0.116 L over 12 weeks). In addition, the mean change from baseline for FEV₁ was greater than about 0.150 L between week 4 through week 12 (generally between about 0.150 L and about 0.250 L). Both doses of BAI were effective in improving asthma control with significantly greater improvements in FEV₁ and morning PEF when compared to placebo. Reduction in asthma symptoms was also supportive of the efficacy of the BAI.

Trial 2: This randomized, double-blind, parallel-group, placebo-controlled, 6-week, efficacy and safety trial compared BAI 40 and 80 mcg BDP given as 4 inhalations twice daily and placebo in adult and adolescent patients with persistent symptomatic asthma despite treatment with non-corticosteroid, inhaled corticosteroids (with or without a long acting beta agonist [LABA]), or combination asthma therapy. The study also included a reference treatment group, QVAR® Inhalation Aerosol (QVAR MDI) 40 mcg, 4 inhalations twice daily. Patients aged 12 years and older who met the entry criteria including FEV₁ 50-90% predicted normal, reversible bronchoconstriction of at least 10% with short-acting inhaled beta-agonist discontinued baseline asthma treatment and entered a 2-4 week run-in period. 425 patients (257 previously treated with ICS with or without LABA) who met all the randomization criteria including FEV₁ of 40-85% predicted and 15% reversibility with short-acting inhaled beta-agonist, and asthma symptoms were randomized equally to the BAI 320 mcg/day, BAI 640 mcg/day, QVAR MDI 320 mcg/day or placebo. Baseline FEV₁ values were similar across treatments. The primary endpoint for this trial was the standardized baseline-adjusted trough morning forced expiratory volume in 1 second (FEV₁) area under the effect curve from time zero to 6 weeks [FEV₁ AUEC(0-6wk)]. Patients in both treatment groups had significantly greater improvements in trough FEV₁ compared to placebo (BAI 320 mcg/day, LS mean change of 0.144 L and BAI 640 mcg/day, LS mean change of 0.150 L over 12 weeks). Treatment with QVAR MDI was similar. The change from baseline in morning FEV₁ during the trial was greater than 0.150 L or 0.200 L between week 2 through week 6 (generally between about 0.150 L and about 0.250 L). Both doses of the BAI were effective in improving asthma control with significantly greater improvements in FEV₁, morning PEF, weekly average of daily trough morning FEV₁, reduced rescue medication use and improved asthma symptom scores than with placebo. Similar results were demonstrated with QVAR MDI.

The inhaler of the present disclosure has broad application. The apparatuses and associated methods in accordance with the present disclosure have been described with reference to particular embodiments thereof in order to illustrate the principles of operation. The above description is thus by way of illustration and not by way of relative and directional references (including: upper, lower, upward, downward, left,

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right, leftward, rightward, top, bottom, side, above, below, front, middle, back, vertical, horizontal, height, depth, width, and so forth) are normally given by way of example to aid the reader's understanding of the particular embodiments described herein. They should not be read to be requirements or limitations, particularly as to the position, orientation, or use of the invention unless specifically set forth in the claims. Connection references (e.g., attached, coupled, connected, joined, secured and the like) are to be construed broadly and may include intermediate members between a connection of elements and relative movement between elements. As such, connection references do not necessarily infer that two elements are directly connected and in fixed relation to each other, unless specifically set forth in the claims.

Various modifications may be made to the embodiments described without departing from the scope of the invention as defined by the accompanying claims.

What is claimed is:

1. A breath actuated inhaler comprising:

a main body for accommodating a medicament reservoir, a canister fire system including a trigger; and

a biasing element for moving a canister to release a dose in response to air flow,

a cap housing,

an interior chamber defined by the main body and the cap housing, the canister fire system and canister being enclosed within the interior chamber, and

a lock system including helical threads having non-overlapping and distinct thread segments for providing rotational attachment of the cap housing to the main body and a first lock member that cooperates with a second lock member to achieve a snap lock between the cap housing and the main body when the cap housing is rotationally attached to the main body in a locked position,

wherein the thread segments are radially disposed about a central axis and arranged such that the thread segments are non-overlapping with respect to each other along the central axis, and

wherein the first lock member is interposed between the thread segments.

2. The breath actuated inhaler of claim 1 wherein, in the locked position, the helical threads provide resistance of longitudinal movement between the cap housing and the main body without rotation.

3. The breath actuated inhaler of claim 1 wherein each of the cap housing and the main body include the thread segments and the lock system includes a protrusion extending from a thread segment on one of the main body and the cap housing which is lockable in a recess of a thread segment on the other of the main body and the cap housing.

4. The breath actuated inhaler of claim 3 wherein the lock system includes a second protrusion extending from a thread segment on one of the main body and the cap housing, the second protrusion being lockable in a second recess of a thread segment on the other of the main body and the cap housing, wherein the recess and the second recess are formed at opposing locations on the inhaler.

5. The breath actuated inhaler of claim 3 wherein a thread segment on one of the cap housing and the main body includes a helical groove, and the protrusion extends from the helical groove.

6. The breath actuated inhaler of claim 3 wherein the thread segment on one of the cap housing and the main body

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includes a radially extending helical protrusion, and the recess is on the radially extending helical protrusion.

7. The breath actuated inhaler of claim 1 wherein the first lock member engages the second lock member along a single face at a lock interface formed by respective engagement faces thereof, the lock interface being oriented substantially perpendicular to tangential.

8. The breath actuated inhaler of claim 7 wherein the first lock member has a radial extent of 0.25 to 0.75 mm and a longitudinal extent of about 10 mm.

9. The breath actuated inhaler of claim 1 in which the main body and the cap housing are formed of plastics material and the lock system is configured so that a release torque required to overcome the lock system is more than 1 Nm.

10. The breath actuated inhaler of claim 9 in which the lock system is configured such that the release torque is between 2 and 5 Nm.

11. A method of treating a respiratory disease or disorder comprising actuating the inhaler of claim 1 to administer a therapeutically effective amount of one or more active ingredients.

12. The method of claim 11, wherein the inhaler is a breath-actuated inhaler and the step of actuating the inhaler comprises inhaling through the inhaler.

13. The method of claim 11, wherein the respiratory disease or disorder is asthma.

14. The method of claim 11, wherein the respiratory disease or disorder is COPD.

15. The method of claim 11, wherein the one or more active ingredients comprise a corticosteroid.

16. The method of claim 11, wherein the one or more active ingredients comprise beclomethasone dipropionate or tiotropium bromide.

17. The breath actuated inhaler of claim 1, wherein the interior chamber comprises a vacuum chamber.

18. The breath actuated inhaler of claim 1, wherein the interior chamber prevents tampering with components within the interior chamber.

19. The breath actuated inhaler of claim 1, wherein the lock system is integrated with the cap housing and main body to resist axial and radial movement of the cap housing relative to the main body.

20. The breath actuated inhaler of claim 1, wherein the cap housing cooperates with the main body to resist axial and radial movement of the cap housing relative to the main body when the lock system is in a locked configuration.

21. The breath actuated inhaler of claim 1, wherein the thread segments are disposed on the cap housing.

22. The breath actuated inhaler of claim 1, wherein the first lock member is disposed on the cap housing and the second lock member is disposed on the main body.

23. The breath actuated inhaler of claim 1, wherein each thread segment has a radial extent that is greater than a radial extent of the first lock member.

24. The breath actuated inhaler of claim 1, wherein the second lock member defines a boundary of a longitudinal cut that is configured and dimensioned to receive the first lock member.

25. The breath actuated inhaler of claim 1, wherein a radial extent of the first lock member is disposed in a same plane as a radial extent of the thread segments.

26. The breath actuated inhaler of claim 1, wherein the first lock member includes a ramp that is inclined relative to a tangent of a radial surface disposed about a central axis.

27. The breath actuated inhaler of claim 26, wherein the ramp includes a terminal end configured to engage the

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second lock member thereby restricting rotation of the cap housing relative to the main body.

28. A breath actuated inhaler comprising: a main body for accommodating a medicament reservoir, a canister fire system for moving a canister to release a dose in response to air flow, a cap housing for enclosing the canister fire system and canister within an interior chamber defined by the main body and the cap housing, and in which the main body and the cap housing are formed of plastics material characterized in that a lock system is provided for locking the cap housing on the main body,

wherein the lock system includes:

helical threads having non-overlapping and distinct thread segments for providing rotational attachment of the cap housing on the main body; and
a first lock member that cooperates with a second lock member to achieve a snap lock between the cap housing and the main body when the cap housing is rotationally attached to the main body in a locked position,

wherein the thread segments are radially disposed about a central axis and arranged such that the thread segments are non-overlapping with respect to each other along the central axis, wherein the first lock member is interposed between the thread segments, and

wherein a release torque required to overcome the lock system is more than 1 Nm and lower than 4 Nm.

29. The breath actuated inhaler of claim 28 wherein, in the locked position, the helical threads provide resistance of longitudinal movement between the cap housing and the main body without rotation.

30. The breath actuated inhaler of claim 28 wherein each of the cap housing and the main body include the thread segments and the lock system includes a protrusion extending from a thread segment on one of the main body and the cap housing which is lockable in a recess of a thread segment on the other of the main body and the cap housing.

31. The breath actuated inhaler of claim 30 wherein the lock system includes a second protrusion extending from a thread segment on one of the main body and the cap housing, the second protrusion being lockable in a second recess of a thread segment on the other of the main body and the cap housing, wherein the recess and the second recess are formed at opposing locations on the inhaler.

32. The breath actuated inhaler of claim 28 wherein the first lock member engages the second lock member along a single face at a lock interface formed by respective engagement faces thereof, the lock interface being oriented substantially perpendicular to tangential.

33. The breath actuated inhaler of claim 32 wherein the first lock member has a radial extent of 0.25 to 0.75 mm and a longitudinal extent of about 10 mm.

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34. A method of treating a respiratory disease or disorder comprising actuating the inhaler of claim 28 to administer a therapeutically effective amount of one or more active ingredients.

35. The method of claim 34, wherein the inhaler is a breath-actuated inhaler and the step of actuating the inhaler comprises inhaling through the inhaler.

36. The method of claim 34, wherein the respiratory disease or disorder is asthma.

37. The method of claim 34, wherein the respiratory disease or disorder is COPD.

38. The method of claim 34, wherein the one or more active ingredients comprise a corticosteroid.

39. The method of claim 34, wherein the one or more active ingredients comprise beclomethasone dipropionate or tiotropium bromide.

40. The breath actuated inhaler of claim 28, wherein the interior chamber comprises a vacuum chamber.

41. The breath actuated inhaler of claim 28, wherein the interior chamber prevents tampering with components within the interior chamber.

42. The breath actuated inhaler of claim 28, wherein the lock system is integrated with the cap housing and main body to resist axial and radial movement of the cap housing relative to the main body.

43. The breath actuated inhaler of claim 28, wherein the cap housing cooperates with the main body to resist axial and radial movement of the cap housing relative to the main body when the lock system is in a locked configuration.

44. The breath actuated inhaler of claim 28, wherein the thread segments are disposed on the cap housing.

45. The breath actuated inhaler of claim 28, wherein the first lock member is disposed on the cap housing and the second lock member is disposed on the main body.

46. The breath actuated inhaler of claim 28, wherein each thread segment has a radial extent that is greater than a radial extent of the first lock member.

47. The breath actuated inhaler of claim 28, wherein the second lock member defines a boundary of a longitudinal cut that is configured and dimensioned to receive the first lock member.

48. The breath actuated inhaler of claim 28, wherein a radial extent of the first lock member is disposed in a same plane as a radial extent of the thread segments.

49. The breath actuated inhaler of claim 28, wherein the first lock member includes a ramp that is inclined relative to a tangent of a radial surface disposed about a central axis.

50. The breath actuated inhaler of claim 49, wherein the ramp includes a terminal end configured to engage the second lock member thereby restricting rotation of the cap housing relative to the main body.

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